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Synthetic enzymes for the production of coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin and vanillic acid and their use

- 5 The present invention relates to <u>synthetic enzymes</u> for the production of coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin and vanillic acid, the use thereof for the production of coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin and vanillic acid, DNA coding for the aforementioned enzymes and microorganisms transformed therewith.
 - The first article relating to the degradation of eugenol was written by Tadasa in 1977 (Degradation of eugenol by a microorganism. Agric. Biol. Chem. 41, 925-929). It describes the degradation of eugenol with a soil isolate which was presumed to be <u>Corynebacterium</u> sp. In this process ferulic acid and vanillin were identified as intermediate degradation products and the subsequent degradation was assumed to proceed via vanillic acid and protocatechuic acid.

In 1983 another article by Tadasa and Kyahara appeared (Initial Steps of Eugenol Degradation Pathway of a Microorganism. Agric. Biol. Chem. 47, 2639-2640) on the initial steps of eugenol degradation, this time with a soil isolate which was identified to be <u>Pseudomonas</u> sp. In this article eugenol oxide, coniferyl alcohol and coniferylaldehyde were described as intermediates for the formation of ferulic acid.

Also in 1983 a report by Sutherland et al. appeared (Metabolism of cinnamic, p-coumaric, and ferulic acids by <u>Streptomyces setonii</u>. Can. J. Microbiol. 29, 1253-1257) on the metabolism of cinnamic, p-coumaric and ferulic acids by <u>Streptomyces setonii</u>. In this process ferulic acid was degraded via vanillin, vanillic acid and protocatechuic acid, the ring-cleaving enzymes catechol 1,2-dioxygenase and protocatechuate 3,4-dioxygenase having been indirectly identified in the cell-free extract.

In 1985 Ötük (Degradation of Ferulic Acid by Escherichia coli. J. Ferment.

Technol. 63, 501-506) reported on the degradation of ferulic acid by a strain of Escherichia coli isolated from decaying bark. Here as well vanillin, vanillic acid and protocatechuic acid were found as degradation products.

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isoeugenol) for the microbial oxidation of eugenol and isoeugenol. However, only when isoeugenol was used the process did produce high conversion rates; the results were very poor using eugenol.

In 1991 EP-A 453 368 appeared ["Production de vanilline par bioconversion de précurseurs benzeniques" (Production of vanillin by the bioconversion of benzene precursors)], in which the reaction to form vanillin from vanillic acid and ferulic acid using a basidiomycete - Pycnoporus cinnabarinus CNCM I-937 and I-938 - was observed

In 1992 the Takasago Perfumery Company was granted a Japanese patent (Preparation of vanillin, coniferyl-alcohol and -aldehyde, ferulic acid and vanillyl alcohol - by culturing mutant belonging to Pseudomonas genus in presence of eugenol which is oxidatively decomposed, JP 05 227 980 21.1.1992) for the preparation of vanillin, coniferyl alcohol, coniferylaldehyde, ferulic acid and vanillyl alcohol from eugenol using a Pseudomonas mutant.

Also in 1992 US Patent No. 5,128,253 by Labuda et al. (Kraft General Foods) (Bioconversion process for the production of vanillin) was granted, in which a biotransformation process for the production of vanillin was described. Here as well the starting material was ferulic acid and the organisms used were Aspergillus niger, Rhodotorula glutinis and Corynebacterium glutamicum. The crucial feature was the use of sulphydryl components (e.g. dithiothreitol) in the medium. In 1993 the subject matter of the patent also appeared in the form of a publication (Microbial bioconversion process for the production of vanillin; Prog. Flavour Precursor Stud. Proc. Int. Conf. 1992, 477-482).

EP-A 542 348 (Process for the preparation of phenylaldehydes) describes a process for the preparation of phenylaldehydes in the presence of the enzyme lipoxygenase. Eugenol and isoeugenol are for example used as substrates. We have attempted to rework the process using eugenol, but have not succeeded in confirming the results of the reactions.

DE-A 4 227 076 [Verfahren zur Herstellung substitutierter Methoxyphenole und dafür geeigneter Mikroorganismus (Process for the production of substituted methoxyphenols and a microorganism suitable for said process)] describes the production of substituted methoxyphenols with a new <u>Pseudomonas</u> sp. The

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starting material used is eugenol and the products are ferulic acid, vanillic acid, coniferyl alcohol and coniferylaldehyde.

Also in 1995 a comprehensive review by Rosazza et al. (Biocatalytic transformation of ferulic acid: an abundant aromatic natural product; J. Ind. Microbiol. <u>15</u>, 457-471) appeared on possible methods of biotransformation using ferulic acid.

The present invention relates to synthetic enzymes for the production of coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin and vanillic acid from eugenol.

Synthetic enzymes according to the invention are for example:

- a) eugenol hydroxylase,
- b) coniferyl alcohol dehydrogenase,
- c) coniferylaldehyde dehydrogenase,
- d) ferulic acid deacylase and
- e) vanillin dehydrogenase.

The invention also relates to DNA coding for the abovementioned enzymes and cosmid clones containing this DNA as well as vectors containing this DNA and microorganisms transformed with the DNA or the vectors. It also relates to the use of the DNA for the transformation of microorganisms for the production of coniferyl alcohol, coniferyladehyde, ferulic acid, vanillin and vanillic acid. The invention also relates to partial sequences of the DNA and functional equivalents. Functional equivalents are understood to be those derivatives in which individual nucleobases have been substituted (wobble substitutions) without resulting in any functional changes. In relation to proteins, amino acids can also be substituted without resulting in any functional changes.

The invention also relates to the individual steps for the production of coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin and vanillic acid from eugenol, i.e. in concrete terms:

 a) the process for the production of coniferyl alcohol from eugenol carried out in the presence of eugenol hydroxylase;

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- the process for the production of coniferylaldehyde from coniferyl alcohol carried out in the presence of coniferyl alcohol dehydrogenase:
- the process for the production of ferulic acid from coniferylaldehyde carried out in the presence of coniferylaldehyde dehydrogenase;
- d) the process for the production of vanillin from ferulic acid carried out in the presence of ferulic acid deacylase;
 - the process for the production of vanillic acid from vanillin carried out in the presence of vanillin dehydrogenase.

After NMG mutagenesis mutants with defects in individual stages of the catabolism of eugenol were obtained from the eugenol-utilising Pseudomonas sp. strain HR 199 (DSM 7063). Using total DNA of wild-type Pseudomonas sp. HR 199 partially digested with EcoRI a gene library was constructed in the pVK100 cosmid, which has a broad host spectrum and can also be replicated in stable form in pseudomonads. After packaging in 1-phage particles the hybrid cosmids were transduced to E. coli S17-1. The gene library comprised 1330 recombinant E. coli S17-1 clones. The hybrid cosmid of each clone was transferred by conjugation into two eugenol-negative mutants (mutants 6164 and 6165) of the Pseudomonas sp. HR 199 strain and tested for a possible capacity for complementation. In this test two hybrid cosmids (pE207 and pE115) were identified, the obtainment of which restored mutant 6165's capacity to utilise eugenol. One hybrid cosmid (pE5-1) resulted in the complementation of mutant 6164.

The complementing capacity of plasmids pE207 and pE115 was attributed to a 23 kbp EcoR1 fragment (E230). A physical map of this fragment was prepared and the fragment completely sequenced. The genes vanA and vanB which code for vanillate demethylase were localised in a 11.2 kbp HindIII subfragment (H110). Another open reading frame (ORF) was found to be homologous to g-glutamyl cysteine synthetase produced by Escherichia coli. An additional ORF, which was homologous to formaldehyde dehydrogenases, was identified between the aforementioned ORF and the vanB gene. Two additional ORF's were found to be homologous to the cytochrome C subunit or the flavoprotein subunit of p-cresol methylhydroxylase, respectively produced by Pseudomonas putida. In the Pseudomonas sp. HR 199 strain, these ORF's code for a new not previously

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described eugenol hydroxylase which converts eugenol into coniferyl alcohol via a quinone methide derivative by a process analogous to the reaction mechanism of p-cresol methyl hydroxylase. Another ORF of an unknown function was identified between the genes of the two subunits of eugenol hydroxylase. An ORF which was homologous to lignostilbene-a,b-dioxygenase was identified in a 5.0 kbp HindIII subfragment (H50). In addition one ORF was identified which was homologous to alcohol dehydrogenases. The structural gene vdh of vanillin dehydrogenase was identified in a 3.8 kbp HindIII/EcoRI subfragment. Upstream of this gene an ORF was localised which was homologous to enoyl-CoA hydratases produced by various organisms.

A eugenol- and ferulic acid-negative mutant (mutant 6167) was complemented by obtaining a 9.4 kbp <u>EcoRI</u> fragment (E 94) of the hybrid cosmid pE5-1. A physical map of this fragment was prepared. The complementing property was localised in a 1.9 kbp <u>EcoRI/HindIII</u> subfragment. This fragment had incomplete ORF's (they extended beyond the <u>EcoRI</u> and <u>HindIII</u> cleavage sites) which were homologous to acetyl-CoA acetyl transferases of various organisms and to the "medium-chain acyl-CoA synthetase" produced by <u>Pseudomonas oleovorans</u>. Fragment E 94 was completely sequenced. Downstream of the aforementioned ORF's an ORF was located which was homologous to \$\beta\$-ketothiolases. The structural gene of coniferylaldehyde dehydrogenase (<u>caldh</u>) was localised in a central position of fragment E 94. Using chromatographic methods the enzyme was isolated from the soluble fraction of the crude extract of cells of <u>Pseudomonas</u> sp. HR 199 grown on eugenol.

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The conjugative transfer of hybrid cosmid pE207 into a large number of Pseudomonas strains resulted in the heterologous expression of the van A, van B and vdh genes and the eugenol-hydroxylase genes in the transconjugants obtained. The obtainment of the plasmid of one strain allowed it to grow using eugenol as its carbon and energy source.

Materials and methods

Growth conditions of the bacteria. Strains of Escherichia coli were grown at 37°C in a Luria-Bertani (LB) or M9 mineral medium (Sambrook, J.E.F. Fritsch and T. Maniatis. 1989. Molecular cloning: a laboratory manual. 2nd Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York). Strains of Pseudomonas sp. and Alcaligenes eutrophus were grown at 30°C in a nutrient broth (NB, 0.8 % by weight) or in a mineral medium (MM) (Schlegel, H. G. et al. 1961. Arch. Mikrobiol. 38: 209-222). Ferulic acid, vanillin, vanillic acid and protocatechuic acid were dissolved in dimethyl sulphoxide and added to the respective medium in a final concentration of 0.1 % by weight. Eugenol was added to the medium directly in a final concentration of 0.1 vol.-%, or applied on filter paper (circular filters 595, Schleicher & Schuell, Dassel, Germany) to the lids of MM agar plates. For the growth of transconjugants of Pseudomonas sp., tetracyline and kanamycin were used in final concentrations of 25 μg/ml and 300 μg/ml, respectively.

Nitrosoguanidine mutagenesis. The nitrosoguanidine mutagenesis of Pseudomonas sp. HR 199 was carried out using a modified method according to Miller (Miller, J. H. 1972. Experiments in molecular genetics. Cold Spring Harbor Laboratory, Cold Spring Harbor, New York). Instead of the citrate buffer, a potassium phosphate (PP) buffer (100 mM, pH 7.0) was used. The final concentration of N-methyl-N'-nitro-N-nitrosoguanidine was 200 µg/ml. The mutants obtained were screened with regard to the loss of their capacity to utilise eugenol, ferulic acid, vanillin and vanillic acid as growth substrates.

Qualitative and quantitative detection of metabolic intermediates in culture supernatants. Culture supernatants were analysed by high-pressure liquid chromatography (Knauer HPLC) either directly or after dilution with twice-distilled water. Chromatography was carried out on Nucleosil-100 C18 (7 μ m, 250 x 4 mm). The solvent used was 0.1 vol.-% formic acid and acetonitrile.

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Purification of coniferyl alcohol dehydrogenase and coniferylaldehyde dehydrogenase. The purification processes were carried out at 4°C.

Crude extract. Cells of <u>Pseudomonas</u> sp. HR 199 grown on eugenol were washed in a 10 mM sodium phosphate buffer with a pH of 7.5, resuspended in the same buffer and disrupted by being passed through a French press (Amicon, Silver Spring, Maryland, USA) twice at a pressure of 1,000 psi. The cell homogenate was subjected to ultracentrifugation (1 h, 100,000 x g, 4°C), the soluble fraction of the crude extract being obtained as the supernatant.

Anion exchange chromatography on DEAE Sephacel. The soluble fraction of the crude extract was dialysed overnight against a 10 mM sodium phosphate buffer with a pH of 7.5 containing 100 mM NaCl. The dialysate was applied to a DEAE Sephacel column (2.6 cm x 35 cm, bed volumn [BV]: 186 ml) equilibrated with a 10 mM sodium phosphate buffer of a pH of 7.5 containing 100 mM NaCl at a flow rate of 0.8 ml/min. The column was washed with two bed volumes of a 10 mM sodium phosphate buffer with a pH of 7.5 containing 100 mM NaCl. The elution of coniferyl alcohol dehydrogenase (CADH) and coniferylaldehyde dehydrogenase (CALDH) was carried out with a linear salt gradient of 100 to 500 mM NaCl in a 10 mM sodium phosphate buffer with a pH of 7.5 (2 x 150 ml). 5 ml fractions were collected. Fractions with high CADH and CALDH activities were combined in the corresponding DEAE pools respectively.

Gel filtration chromatography on Sephadex G200. The CADH DEAE pool was concentrated in a 50 ml Amicon ultrafiltration chamber via a Diaflo ultrafiltration membrane PM 30 (both from AMICON CORP., Lexington, USA) at a pressure of 290 kPa to a volume corresponding to approx. 2% of the Sephadex G200-BV. The concentrated protein solution was applied to a Sephadex G200 column (BV: 138 ml) equilibrated with a 10 mM sodium phosphate buffer with a pH of 7.5 containing 100 mM NaCl and eluted with the same buffer at a flow rate of 0.2 ml/min. 2 ml fractions were collected. Fractions with a high CADH activity were combined in the Sephadex G200 pool.

Hydrophobic interaction chromatography on butyl Sepharose 4B. The CADH Sephadex G200 pool was adjusted to 3 M NaCl and then applied to a butyl Sepharose 4B column (BV: 48 ml) equilibrated with a 10 mM sodium phosphate buffer with a pH of 7.5 containing 3 M NaCl (flow rate: 0.5 ml/min). The

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column was then washed with 2 BV of a 10 mM sodium phosphate buffer with a pH of 7.5 containing 3 M NaCl (flow rate: 1.0 ml/min). CADH was eluted with a linearly decreasing NaCl gradient of 3 to 0 M NaCl in a 10 mM sodium phosphate buffer with a pH of 7.5 (2 x 50 ml). 4 ml fractions were collected. Fractions with a high CADH activity were combined in the HIC pool and concentrated as described above.

Chromatography on hydroxyapatite. The CALDH DEAE pool was concentrated to 10 ml in a 50 ml Amicon ultrafiltration chamber via a Diaflo ultrafiltration membrane PM 30 (both from AMICON CORP., Lexington, USA) at a pressure of 290 kPa. The concentrated protein solution was applied to a hydroxyapatite column (BV: 80 ml) equilibrated with a buffer (10 mM NaCL in a 10 mM sodium phosphate buffer with a pH of 7.0) (flow rate: 2 ml/min). The column was then washed with 2.5 bed volumes of a buffer (flow rate: 2 ml/min). CALDH was eluted with a linearly increasing sodium phosphate gradient of 10 to 400 mM NaP (in each case containing 10 mM NaCL) (2 x 100 ml). 10 ml fractions were collected. Fractions with high CALDH activity were combined in the CALDH HA pool.

Gel filtration chromatography on Superdex HR 200 10/30. The CALDH HA pool was concentrated to 200 μ l (Amicon ultrafiltration chamber, ultrafiltration membrane PM 30) and applied to a Superdex HR 200 10/30 column (BV: 23.6 ml) equilibrated with a 10 mM sodium phosphate buffer with a pH of 7.0. CALDH was eluted with the same buffer at a flow rate of 0.5 ml/min. 250 μ l fractions were collected. Fractions with high CALDH activity were combined in the CALDH Superdex pool.

Determination of coniferyl alcohol dehydrogenase activity. The CADH activity was determined at 30°C by means of an optical enzymatic test according to Jaeger et al. (Jaeger, E., L. Eggeling and H. Sahm. 1982. Current Microbiology. 6: 333-336) with the aid of a ZEISS PM 4 spectrophotometer fitted with a TE converter (both from ZEISS, Oberkochen, Germany) and a recorder. The reaction mixture with a volume of 1 ml contained 0.2 mmol of Tris/HCl (pH 9.0), 0.4 μ mol of coniferyl alcohol, 2 μ mol of NAD, 0.1 mmol of semicarbazide and a solution of the enzyme ("Tris" = tris(hydroxymethyl)-aminomethane). The reduction of NAD was monitored at l=340 nm (e = 6,3 cm²/ μ mol). The enzyme activity was recorded in units (U), 1 U corresponding to that quantity of enzyme

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which metabolises 1 µmol of substrate per minute. The protein concentrations in the samples were determined according to the method described by Lowry et al. (Lowry, O.H., N.J. Rosebrough, A.L. Farr and R. J. Randall. 1951. J. Biol. Chem. 193; 265-275).

Determination of the coniferylaldehyde dehydrogenase activity. The CALDH activity was determined at 30°C by an optical enzymatic test with the aid of a ZEISS PM 4 spectrophotometer fitted with a TE converter (both from ZEISS, Oberkochen, Germany) and a recorder. The reaction mixture of a volume of 1 ml contained a 10 mM Tris/HCl buffer (pH 8.8), 5.6 mM coniferylaldehyde, 3 mM NAD and a solution of the enzyme. The oxidation of coniferylaldehyde to form ferulic acid was monitored at l=400 nm (e = 34 cm²/µmol). The enzyme activity was recorded in units (U), 1 U corresponding to that quantity of enzyme which metabolises 1 µmol of substrate per minute. The protein concentration in the samples was determined according to the method described by Lowry et al. (Lowry, O.H., N.J. Rosebrough, A.L. Farr and R. J. Randall. 1951. J. Biol. Chem. 193: 265-275).

Electrophoretic methods. The separation of protein-containing extracts was carried out in 7.4% by weight polyacrylamide gels under native conditions according to the method described by Stegemann et al. (Stegemann et al. 1973. Z. Naturforsch. 28c: 722-732) and under denaturing conditions in 11.5 % by weight polyacrylamide gels according to the method described by Laemmli (Laemmli, U.K. 1970. Nature (London) 227: 680-685). Serva Blue R was used for nonspecific protein staining. For specifically staining coniferyl alcohol, coniferylaldehyde and vanillin dehydrogenase the gels were placed for 20 mins in a new 100 mM PP buffer (pH 7.0) and then incubated at 30°C in the same buffer, to which 0.08 % by weight of NAD, 0.04 % by weight of p-nitroblue-tetrazolium chloride, 0.003 % by weight of phenazine methosulphate and 1 mM of the respective substrate had been added, until the corresponding coloured bands appeared.

The transfer of proteins from polyacrylamide gels to PVDF membranes. Proteins were transferred from SDS polyacrylamide gels to PVDF membranes (Waters-Milipore, Bedford, Mass., USA) with the aid of a semidry fast blot device (B32/33 from Biometra, Göttingen, Germany) according to the manufacturer's instructions.

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Determination of N-terminal amino acid sequences. The determination of N-terminal amino acid sequences was carried out with the aid of a protein peptide sequencer (of type 477 A, Applied Biosystems, Foster City, USA) and a PTH analyser according to the manufacturer's instructions.

Isolation and manipulation of DNA. The isolation of genomic DNA was carried out by the method described by Marmur (Marmur, J. 1961. Mol. Biol. 3: 208-218). Megaplasmid DNA was isolated according to the method described by Nies et al. (Nies, D., et al. 1987. J. Bacteriol. 169: 4865-4848). The isolation and analysis of other plasmid DNA or DNA restriction fragments, the packaging of hybrid cosmids in l-phage particles and the transduction of E. coli. was carried out by standard methods (Sambrook, J.E.F. Fritsch and T. Maniatis. 1989. Molecular cloning: a laboratory manual. 2nd Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York).

Transfer of DNA. The preparation and transformation of competent Escherichia coli cells was carried out by the method described by Hanahan (Hanahan, D. 1983, J. Mol. Biol. 166: 557-580). Conjugative plasmid transfer between plasmid-containing Escherichia coli S17-1 strains (donor) and Pseudomonas sp. strains (recipient) and Alcaligenes eutrophus (recipient) was carried out on NB agar plates according to the method described by Friedrich et al. (Friedrich, B. et al. 1981, J. Bacteriol. 147: 198-205) or by a "minicomplementation method" on MM agar plates using 0.5 % by weight of gluconate as the carbon source and 25 μg/ml of tetracylin or 300 μg/ml of kanamycin. In this process cells of the recipient were applied in one direction in the form of an inoculation line. After 5 minutes cells of the donor strains were then applied in the form of inoculation lines crossing the recipient inoculation line. After incubation for 48 h at 30°C the transconjugants grew directly downstream of the crossing point, whereas neither the donor nor the recipient strain was capable of growth.

Hybridisation experiments. DNA restriction fragments were electrophoretically separated in an 0.8 % by weight agarose gel in a 50 mM Tris, 50 mM boric acid and 1.25 mM EDTA buffer (pH 8.5) (Sambrook, J.E.F. Fritsch and T. Maniatis. 1989. Molecular cloning: a laboratory manual. 2nd Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York). The transfer of the denatured DNA from the gel to a positively charged nylon membrane (pore size: 0.45 µm, Pall Filtrationstechnik, Dreieich, Germany), the subsequent hybridisation with

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biotinylated or ³²P-labelled DNA probes and the production of these DNA probes was carried out according to standard methods (Sambrook, J.E.F. Fritsch and T. Maniatis. 1989. Molecular cloning: a laboratory manual. 2nd Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York).

The synthesis of oligonucleotides. Using desoxynucleoside phosphoramidites as the starting material, oligonucleotides were synthesised on a 0.2 μ mol scale (Beaucage, S. L., and M. H. Caruthers. 1981. Tetrahedron Lett. 22: 1859-1862). The synthesis was carried out in a Gene Assembler Plus according to the manufacturer's instructions (Pharmacia-LKB, Uppsala, Sweden). The elimination of the protecting groups was carried out by incubation for 15 h at 55°C in a 25 vol.-% aqueous ammonia solution. The oligonucleotides were finally purified in an NAP-5 column (Pharmacia-LKB, Uppsala, Sweden).

DNA sequencing. The determination of nucleotide sequences was carried out by the didesoxy chain termination method described by Sanger et al. (Sanger et al. 1977. Proc. Natl. Acad. Sci. USA 74: 5463-5467) using

 α^{-35} SldATP and a T7 polymerase sequencing kit (Pharmacia-LKB). 7-Deazaguanosine-5'-triphosphate was used instead of dGTP (Mizusawa, S. et al. 1986. Nucleic Acids Res.14: 1319-1324). The products of the sequencing reactions were separated in a 6% by weight polyacrylamide gel in a 100 mM Tris/HCl, 83 mM boric acid and 1 mM EDTA buffer (pH 8.3) containing 42 % by weight urea, an S2 sequencing apparatus (GIBCO/BRL, Bethesda Research Laboratories GmbH, Eggenstein, Germany) being used according to the manufacturer's instructions. After electrophoresis the gels were incubated for 30 mins in 10 vol.-% acetic acid and, after washing briefly in water, dried for 2 hours at 80°C. Kodak X-OMAT AR X-ray films (Eastman Kodak Company, Rochester, NY, USA) were used for the autoradiography of the dried gels. In addition DNA sequences were also determined "non-radioactively" with the aid of an "LI-COR DNA Sequencer Model 4000L" (LI-COR Inc., Biotechnology Division, Lincoln, NE, USA) using a "Thermo Sequenase fluorescent labelled primer cycle sequencing kit with 7-deaza-dGTP" (Amersham Life Science, Amersham International plc, Little Chalfont, Buckinghamshire, England), in each case according to the manufacturer's instructions.

Various sequencing strategies were used: With the aid of synthetic oligonucleotides sequencing was carried out by the "Primer-hopping Strategy" described by

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Strauss et al. (Strauss, E. C. et al. 1986. Anal. Biochem. 154: 353-360). If only "universal" and "reverse primers" were used hybrid plasmids were used as "template DNA", the inserted DNA fragments of which had been unidirectionally shortened with the aid of an "Exo III/Mung Bean Nuclease Deletion" kit (Stratagene Cloning Systems, La Jolla, Cal., USA) according to the manufacturer's instructions.

Chemicals, biochemicals and enzymes: Restriction enzymes, T4 DNA ligase, lambda DNA and enzymes and substrates for the optical enzymatic tests were obtained from C. F. Boehringer & Söhne (Mannheim, Germany) or from GIBCO/BRL (Eggenstein, Germany). [a-35S]dATP and [g-32P]ATP were obtained from Amersham/Buchler (Braunschweig, Germany). NA-type agarose was obtained from Pharmacia-LKB (Uppsala, Sweden). All the other chemicals were from Haarmann & Reimer (Holzminden, Germany), E. Merck AG (Darmstadt, Germany), Fluka Chemic (Buchs, Switzerland), Serva Feinbiochemica (Heidelberg, Germany) or Sigma Chemie (Deisenhofen, Germany)

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Examples

Example 1

The isolation of mutants of the <u>Pseudomonas</u> sp. HR 199 strain with defects in the catabolism of eugenol

The <u>Pseudomonas</u> sp. HR 199 strain was subjected to nitrosoguanidine mutagenesis in order to isolate mutants with defects in the catabolism of eugenol. The mutants obtained were classified according to their capacity to utilise eugenol, ferulic acid and vanillin as their carbon and energy source. Mutants 6164 and 6165 were no longer capable of utilising eugenol as a carbon and energy source, although, as in the case of the wild type, they were capable of utilising eugenol and vanillin. Mutants 6167 and 6202 were no longer capable of utilising eugenol and ferulic acid as their carbon and energy source, although, as in the case of the wild type, they were capable of utilising vanillin. The abovementioned mutants were used in the subsequent molecular-biological analyses.

Example 2

Construction of a <u>Pseudomonas</u> sp. HR 199 gene library in the cosmid vector pVK100

The genomic DNA of the <u>Pseudomonas</u> sp. HR 199 strain was isolated and subjected to partial restriction digestion with <u>Eco</u>RI. The DNA preparation thus obtained was ligated with vector pVK100 cut by <u>Eco</u>RI. The DNA concentrations were relatively high in order to accelerate the formation of concatemeric ligation products. The ligation materials were packaged in 1-phage particles which were subsequently used for transduction of <u>E. coli</u> S17-1. The selection of the transductants was carried out on tetracycline-containing LB agar plates. In this manner 1330 transductants were obtained which contained various hybrid cosmids.

Example 3

The identification of hybrid cosmids containing essential genes of eugenol catabolism

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The hybrid cosmids of the 1330 transductants were transferred conjugatively to mutants 6164 and 6165 by a minicomplementation process. The resulting transconjugants were examined on MM plates containing eugenol for their capacity to grow again on eugenol (complementation of the respective mutant). Mutant 6164 was complemented by the obtainment of hybrid cosmid pE5-1, which contained a 1.2 kbp, a 1.8 kbp, a 3 kbp, a 5.8 kbp and a 9.4 kbp EcoRI fragment in cloned form. The E. coli S17-1 strain containing this hybrid cosmid was deposited at the "Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH" (DSM) under the number DSM 10440. Mutant 6165 was complemented by the obtainment of the hybrid cosmids pE207 or pE115 respectively. The complementing capacity was attributed to a 23 kbp EcoRI fragment which was contained in cloned form in the hybrid cosmid pE207 as the only EcoRI fragment, whereas hybrid cosmid pE115 additionally contained a 3 kbp and a 6 kbp EcoRI fragment. The E. coli S17-1 strain containing hybrid cosmid pE207 was deposited at the DSM under the number DSM 10439.

Example 4

The analysis of the 23 kbp EcoRI fragment (E230) of the hybrid cosmid pE207

Fragment E230 was isolated preparatively from <u>EcoRI-digested</u> hybrid cosmid pE207 and ligated to pBluescript SKT-DNA digested with <u>EcoRI</u>. Using the ligation material <u>EcoRI</u> XL1-Blue was transformed. Following "blue-white" selection on LB-Tc-Amp agar plates containing X-Gal and IPTG, "white" transformants were obtained whose hybrid plasmids pSKE230 contained the fragment E230 in cloned form. With the aid of this plasmid and by using various restriction enzymes a physical map of the fragment E230 was prepared (Fig. 1).

By cloning subfragments of E230 in vectors pVK101 and pMP92, both of which have a broad host specturm and are also stable in pseudomonads, followed by conjugative transfer into mutant 6165, the region complementing mutant 6165 was localised in a 1.8 kbp Kpnl fragment (K18). After cloning this fragment in pBluescript SK⁻ the nucleotide sequence was determined, the gene of the cytochrome C subunit of eugenol hydroxylase being identified. The gene product of 117 amino acids had an N-terminal leader peptide (MMNVNYKAVGAS-LLLAFISQGAWA) and 32.9% identity (via a region of 82 amino acids) with the

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cytochrome C subunit of p-cresol methylhydroxylase produced by Pseudomonas putida (McIntire et al. 1986, Biochemistry 25:5975-5981).

By cloning the KpnI subfragments of E230 adjacent to K18 in pBluescript SKand sequencing, additional open reading frames (ORF) were identified, one of which codes for the flavoprotein subunit of eugenol hydroxylase and was highly homologous to the flavoprotein subunit of p-cresol methylhydroxylase produced by Pseudomonas putida. An additional ORF was found to be highly homologous to g-glutamyl cysteine synthetase (the first enzyme in the biosynthesis of glutathione) produced by Escherichia coli (Watanabe et al. 1986. Nucleic Acids Res. 14: 4393-4400).

In the soluble fraction of the crude extract of E. coli (pSKE230) vanillin dehydrogenase was detected by specific activity staining in a polyacrylamide gel. By subcloning in pBluescript SK- and analysis of soluble fractions of the crude extracts of the transformants obtained, the vanillin dehydrogenase gene (vdh) was localised in a 3.8 kbp HindIII/EcoRI subfragment of E230. nucleotide sequence of this fragment was determined. The molecular weight of the vanillin dehydrogenase was 50,779, as confirmed by SDS polyacrylamide gel The amino acid sequence was highly homologous to other electrophoresis. aldehyde dehydrogenases of various origins.

Upstream of the vdh gene an additional ORF was identified which was homologous to enoyl-CoA hydratases. The calculated molecular weight of 27,297 was confirmed by SDS polyacrylamide gel electrophoresis.

By sequencing the 5.0 kbp HindIII subfragment of E230, which had also been cloned in pBluescript SK, an ORF was identified which was highly homologous to the lignostilbene-a,b-dioxygenase produced by Pseudomonas paucimobilis. By complete sequencing of the fragment E230 two additional ORF's were identified which were homologous to formaldehyde-dehydrogenases (fdh) and alcohol dehydrogenases (adh) (cf. Fig. 1).

The analysis of the region of hybrid cosmid pE5-1 complementing mutant 6164

Mutant 6164 was complemented by the obtainment of hybrid cosmid pE5-1 which contained a 1.2 kbp (E12), a 1.8 kbp (E18), a 3 kbp (E30), a 5.8 kbp (E58) and a 9.4 kbp (E94) EcoRI fragment in cloned form (Fig. 1). By digesting pE5-1 with EcoRI and subsequent religation a derivative (pE106) of this hybrid cosmid was obtained which only contained fragments E12, E18 and E30. Following conjugative transfer into mutant 6164 this plasmid was however capable of complementing the latter, as a result of which corresponding transconjugants were once again capable of growing on eugenol as a carbon and energy source.

After digesting plasmid pE106 with <u>Eco</u>RI, gel-electrophoretic separation of the digestion material in a 0.8 % by weight agarose gel and transfer of the DNA to a nylon membrane, hybridisation was carried out with a ³²P-labelled oligonucleotide probe of the following sequence:

Agi

	2		6	<u>_</u>	^,	47	
CAA	CTC	ACC	AAC	AAA	AAA	ATC	GT-3'
G	G	C	T	G	G	T	
G	G	C		G	G		
G	T	G		G	G		
		G		G	G		
		T		G	G		
	G G	CAA CTC G G	CAA CTC ACC G G C G G C G T G	CAA CTC ACC AAC G G C T G G C G G T G F	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	G G C G G G G G G G

The sequence of this gene probe had been deduced from the N-terminal amino acid sequence of coniferyl alcohol dehydrogenase (CADH) (see below) purified from Pseudomonas sp. HR 199. With the aid of this probe the region of the cadh gene encoding the N-terminus of the CADH was localised in fragment E12. This fragment and parts of the adjacent fragment E 18 were also sequenced and the complete sequence of the cadh gene thus determined. The amino acid sequence deduced from cadh was homologous to other alcohol dehydrogenases of class I, group II (according to Matthew and Fewson. 1994. Critical Rev. Microbiol. 20(1): 13-56).

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Example 6

Purification and characterisation of coniferyl alcohol dehydrogenase

<u>Pseudomonas</u> sp. HR 199 was grown on eugenol. The cells were harvested, washed and disrupted with the aid of a French press. The soluble fraction of the crude extract obtained after ultracentrifugation had a specific activity of 0.24 U/mg of protein. By means of chromatography on DEAE Sephacel an 11.7-fold enrichment of CADH was obtained in a yield of 83.7 %. By means of chromatography on Sephadex G200 a 6.8-fold enrichment of CADH was obtained in a yield of 11.2 %. By means of chromatography on butyl Sepharose 4B a 70.6-fold enrichment of CADH was obtained in a yield of 7.8 %.

With the aid of this method a preparation was obtained which displayed a band at 27 kDa according to SDS polyacrylamide gel electrophoresis. The purification factor was 64 and the yield 0.8 %.

Optimum temperature and thermal stability

The optimum temperature for the reaction catalysed with CADH was 42°C. The enzyme was however sensitive to heat. The half-lives were as follows: $T_{1/2}$ (34°C) = 5 mins, $T_{1/2}$ (39°C) = 1 min, $T_{1/2}$ (42°C) <1 min.

Optimum pH

The optimum pH for the reaction catalysed by CADH was 10.9 in a 25 mM MOPS buffer. At higher pH values a decrease in activity due to denaturation was observed

Apparent molecular weight

The molecular weight of native CADH was determined with the aid of FPLC by gel filtration on Superdex 200HR 10/30 at 54.9 kDa, which suggests a a₂ subunit structure.

N-terminal amino acid sequence

The determination of the N-terminal amino acid sequence of the purified protein revealed the following result:

(Sequence in the single letter code; ?: definition not possible; (): not certain; in the second row an amino acid is mentioned which may also apply)

Example 7

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Purification and characterisation of coniferylaldehyde dehydrogenase

<u>Pseudomonas</u> sp. HR 199 was grown on eugenol. The cells were harvested, washed and disrupted with the aid of a French press. The soluble fraction of the crude extract obtained after ultracentrifugation displayed a specific activity of 0.43 U/mg protein. By chromatography on DEAE Sephacel a 6.6-fold enrichment of CALDH was obtained in a yield of 65.3 %. By chromatography on hydroxyapatite a 63-fold enrichment of CALDH was obtained in a yield of 33 %. By chromatography on Superdex HR 200 an 81-fold enrichment of CALDH was obtained in a yield of 13 %. With the aid of this method a preparation was obtained which, according to SDS polyacryamide gel electrophoresis, displayed a band at approx. 49 kDa.

20 Optimum temperature and thermal stability

The optimum temperature of the reaction catalysed by CALDH was 26°C. The enzyme was sensitive to heat. The half-lives were as follows: $T_{1/2}~(31^{\circ}C) = 5~\text{mins},~T_{1/2}~(34^{\circ}C) = 2.5~\text{mins},~T_{1/2}~(38^{\circ}C) = 1~\text{min}.$

Optimum pH

25 The optimum pH for the reaction catalysed by CALDH was 8.8 in a 100 mM Tris/HCl buffer. At this pH value the enzyme is however already unstable (87 % decrease in activity within 5 mins). At lower pH values the enzyme is more stable (e.g. pH 6.0: 50 % decrease in activity within 4 hours).

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Substrate specificity

The enzyme not only accepts coniferylaldehyde (100 %) but also transcinnamaldehyde (96.7 %), sinapyl aldehyde (76.7 %), p-anisaldehyde (23.1 %), benzaldehyde (17.8 %), 3,5-dimethoxy-benzaldehyde (7.6 %) and 3-hydroxy-benzaldehyde (1.7 %) as substrates.

The K_M value of CALDH for coniferylaldehyde is in the range between 0.007 and 0.012 mM at a V_{max} of approx. 9 to 15 U/ml. The K_M value of CALDH for NAD is 0.334 mM at a V_{max} of 14.2 U/ml. Compared with NAD, NADP is accepted at a rate of 4.3 %.

N-terminal amino acid sequence

The determination of the N-terminal amino acid sequence of the purified protein revealed the following result:

ISILGLNGAPVGAEQLGSAL(D) 20

(sequence in the one-letter code; (): not certain).

Example 8

Localisation and sequencing of the coniferylaldehyde dehydrogenase gene (caldh)

The N-terminal amino acid sequence was definitively assigned to an amino acid sequence deduced from the DNA sequence of fragment E94 of plasmid pE5-1. Thus the CALDH structural gene <u>caldh</u> is localised in E94. The amino acid sequence deduced from <u>caldh</u> was homologous to other aldehyde dehydrogenases.

Example 9

The complementation of other mutants displaying defects in the catabolism of eugenol using hybrid cosmids pE207 and pE5-1 $\,$

Following NMG mutagenesis, mutants 6167 and 6202 had been obtained which were no longer capable of utilising eugenol and ferulic acid as their carbon and energy source (see above). The obtainment of plasmid pE207 meant that, after

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conjugative transfer, mutant 6202 was once again capable of utilising the aforementioned substrates. This mutant is complemented by the gene homologous to enoyl-CoA hydratase.

The obtainment of plasmid pE5-1 meant that, after conjugative transfer, mutant 6167 was once again capable of utilising the abovementioned substrates. By individually cloning the EcoRI fragments of pE5-1 in pHP 1014 and the conjugative transfer of these plasmids into mutant 6167 the complementing property was localised in fragment E94. A physical map of fragment E94 was prepared after cloning in pBluescript SK and digestion with various restriction enzymes. By cloning subfragments of E94 in the vectors pVK101 and pMP92, followed by conjugative transfer into mutant 6167, the region complementing mutant 6167 was localised in a 1.9 kbp EcoRI/HindIII fragment (EH19). After cloning this fragment in pBluescript SK and sequencing, 2 ORF's were identified which were homologous to acetyl-CoA acetyltransferases and to "medium-chain acyl-CoA synthetase" produced by Pseudomonas oleovorans. By completely sequencing fragment E94, additional ORF's were identified which were homologous to regulator proteins and a chemotaxis protein (cf. Fig. 1).

Example 10

Determination of the chromosomal coding of the genes for the catabolism of eugenol in <u>Pseudomonas</u> sp. HR 199

Since <u>Pseudomonas</u> sp. HR 199 has a megaplasmid of a size of approx. 350 kbp, a hybridisation experiment was carried out to examine whether the genes for the catabolism of eugenol were localised in this megaplasmid or in the chromosome. For this purpose megaplasmid preparations of the wild type and of the mutants were separated in an 0.8 % by weight agarose gel. The chromosomal and megaplasmid DNA was blotted onto a nylon membrane and then hybridised against a biotinylated HE38 DNA probe. A hybridisation signal was only obtained with the chromosomal DNA and not with the megaplasmid DNA. Thus the genes for the catabolism of eugenol in <u>Pseudomonas</u> sp. HR 199 are coded in the chromosome.

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Example 11

The heterologous expression of genes for the catabolism of eugenol from Pseudomonas sp. HR 199 in other Pseudomonas strains and in Alcaligenes eutrophus.

The plasmid pE207 and a pVK101 hybrid plasmid containing fragment H110 (pVKH110) were conjugatively transferred to A. <u>eutrophus</u> and into <u>Pseudomonas</u> strains which were not capable of metabolising eugenol, vanillin or vanillic acid. The transconjugants obtained were not only examined for their capacity to grow on MM agar plates containing eugenol, vanillin or vanillic acid but also some transconjugants were incubated with eugenol in an MM liquid medium. By means of HPLC analysis of the culture supernatants some of the transconjugants were found to metabolise eugenol.

In this analysis the functional expression of the <u>vdh</u> gene in transconjugants of <u>P. stutzeri</u>, <u>P. asplenii</u>, <u>Pseudomonas</u> sp. DSM13, <u>Pseudomonas</u> sp. DSM15a and <u>Pseudomonas</u> sp. D1 was determined.

Transconjugants of the strain <u>Pseudomonas</u> sp. D1, which contained the plasmid pE207, were capable of growing using eugenol as their carbon and energy source. In corresponding transconjugants of <u>P. testosteroni</u> LMD3324, <u>P. fluorescens</u> TypeB, <u>P. stutzeri</u> DSM 50027, <u>Pseudomonas</u> sp. DSM 1455 and <u>P. fragi</u> DSM3456 functional expression of the eugenol hydroxylase genes was also observed which resulted in the secretion of intermediates of the catabolism of eugenol (coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin, vanillic acid) into the culture medium. Growth of these transconjugants on eugenol was however not observed.

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SEQUENCE LISTING

	TNFORMATTON

- (i) APPLICANT:
 - (A) NAME: Haarmann & Reimer GmbH
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 - (F) POSTAL CODE (ZIP): 37603
 - (G) TELEPHONE: 0214-3067988
 - (H) TELEFAX: 0214-303482
- (ii) TITLE OF INVENTION: Syntheseenzyme fuer die Herstellung von Coniferylalkohol, Coniferylaldehyd, Ferulasaeure, Vanillin und Vanillinsaeure und deren Verwendung
- (iii) NUMBER OF SEQUENCES: 42
- (iv) COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Floppy disk
 - (B) COMPUTER: IBM PC compatible
 - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
- (D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)
- (2) INFORMATION FOR SEQ ID NO: 1:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32679 base pairs
 - (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Pseudomonas sp.
 - (B) STRAIN: HR199
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 3146..3997
 - (D) OTHER INFORMATION:/gene= "ORF1"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:



AGCGTGCATC CGGATCGGTG AGTGAGACTT GCCCATCCGG TGCTTCACGT AGCTGCTGCT 1800 CCATCTCCTT GAGCGCCTGC ATCTGCTGGC GGAGTTTCTC GATTTTATCC TGGAGGCGGC 1860 TGGCTTTGGC TTCGGCGACA TCGGATTGAG TTCTGTCGGC GGTGTCCATC GCTGCCAGAT 1920 AGCGGTCGAT GATTTTATCA ATCTGGTCCA TCCGGGCGCG CACCCGCTAT GATCCGGAGT 1980 CCTCCGATAT CGATGAGGCC TATCTGGGCT GGAAGAGCGG TTCGGTGTTC TCAGACCTTG 2040 GCGAGAACGC GGTCAAGCTC AGCTTCGGGC GCCAAGCCTT CAAGATCGGC AACGGCTTCC 2100 TGATCGGCGA AGGCCACGTC GACCAAGGTA ACGATGCGGG CTACTGGCTG GCCCCTACCT 2160 AGGCGTTCGA CAACACCGTC CTAGCCCAAC TGGACACCGG CAAGCTGCAT GTCGACCTGT 2220 TCGACCTCCA GGCGGGCATG GATCTGGACG TCGCCGACAT CAAGGAGAAA GTCCGGGTGC 2280 GCGGGGGCAA CGTCGAGTGG CGCGACGAGA CCTACGGCAC GGTAGGGTTC ACCGGCTTCC 2340 ATACGCTGGA CGCTGACAAT CCGCTGCGCG ACGGCATGAA TGTCTACGAC GTACGCGCAT 2400 CGGGCAGCCC GATCCGAGCC CTGCCGCAGG TGGCCCTGGC GGCGGAGTAC GCCTGGCAGC 2460 GCGGCGGCGA GGCGGACAAG ACGAGTGAGG CCTGGTACCT ACAGGGCAGC TACACCTTTC 2520 GGGATGCCCC CTGGACGCCA GTGCTGATGT ACCGTCACGC GGTCTTCTCC GACGACTACG 2580 ACTCCCTGCT GTACGGCTAA GGGGGCAACA ACATGGGCTG GAAAGGAGCA TTGCGTTGAA 2640 ACGATGCTGA AGGGCGTCAC TCTTTTACTG CTGTCCGCTC ACGTCGAAAC TGCATGATTT 2700 CGGGCAGCCT TTCTTCTATC CAGTCGGCCA GCACCTGAAC ATGAGCCGCT ACTTCCTGGC 2760 CAAGCGGCGT CAGGCTGTAC TCGACATGTG GGGGAACGAC CGGGAGCGAA TGTCGAGCTA 2820 TGAAACCGTC TCCCTCCAGG CCTTGTAGGG TCTGCGCAAG CATTCTTTTC GCTGACACCG 2880 CCGATTCTTC CGACGCAGGT CGCTGAATCG ATGGACACCG TCCACCAAGA TGATCAGCAC 2940 GAGCACGCCC AGCGGCTTGT CACGTGCTTG AGCACGTCCC GCGACGGCAT TCAGCACTCA 3000 GCAATTCCCG CGCCGTGCTT GCATGGAGAG ACTGGTAAGG GCGGCCAGCG TGAGTTTCAT 3060 GGCACTAACC TTTATGTATG TACTTACTTT TAGTTGCTAG TAGGGATATG GTGACGCCTT 3120 CATCCTACGA AACAAGTGAA GACTG ATG ATC GCC ATC ACA GGT GCC TCC GGA 3172 Met Ile Ala Ile Thr Glv Ala Ser Glv CAA CTT GGT CGG TTG ACT ATA GAG GCG CTA CTG AAG CGC CTG CCA GCA 3220 Gln Leu Gly Arg Leu Thr Ile Glu Ala Leu Leu Lys Arg Leu Pro Ala 10 20

TC0 Se1	GA#	ATT	r ATT	GCC Ala	Leu	GTC Val	CGG Arg	GAT Asp	CCG Pro 35	Asn	'AAG Lys	GCC Ala	GGA Gly	GAC Asp 40	CTT Leu	3268
Thr	GCA Ala	Arq	GGC Gly Gly 45	7 Il∈	GTG Val	GTG Val	Arg	Gln 50	GCC	GAT Asp	TAC	AAC Asn	CGG Arg 55	CCG	GAA Glu	3316
AC# Thr	CTC	CAC His	C CGG Arg	GCC Ala	CTG Leu	ATT	GGG Gly 65	GTC Val	AAC Asn	CGG Arg	TTG Leu	CTG Leu 70	Leu	ATT	TCC Ser	3364
TCC	AGT Ser 75	Glu	GTG Val	GGT Gly	CAA Gln	CGA Arg 80	ACT Thr	GCG Ala	CAA Gln	CAC	CGG Arg 85	GCA Ala	GTG Val	ATC Ile	GAC Asp	3412
GCT Ala 90	GCG Ala	AAG Lys	GAA	GAA Glu	GGT Gly 95	ATC Ile	GAG Glu	TTG Leu	CTG Leu	GCT Ala 100	TAT	ACG Thr	AGT Ser	CTG Leu	CTT Leu 105	3460
CAT	GCC Ala	GAT Asp	AAA Lys	TCG Ser 110	GCG Ala	CTG Leu	GGC Gly	CTA Leu	GCG Ala 115	ACT Thr	GAA Glu	CAC His	CGA Arg	GAC Asp 120	ACG Thr	3508
GAA Glu	CAG Gln	GCC	Leu 125	ACA Thr	GAG Glu	TCC Ser	GGT Gly	ATT Ile 130	CCT Pro	CAT His	GTC Val	CTG Leu	TTG Leu 135	CGC Arg	AAC Asn	3556
			CAC His													3604
CAT His	GGC Gly 155	GTG Val	TTG Leu	CTG Leu	GGC Gly	TGT Cys 160	GCC Ala	CAG Gln	GAT Asp	GGC Gly	TTG Leu 165	ATT Ile	GCT Ala	TCT Ser	GCT Ala	3652
GCA Ala 170	CGT Arg	GCT Ala	GAC Asp	TAC Tyr	GCC Ala 175	GAA Glu	GCA Ala	GCG Ala	GCT Ala	GTG Val 180	GTG Val	CTC Leu	ACC Thr	GGT Gly	GAG Glu 185	3700
AAT Asn	CAG Gln	GCA Ala	GGT Gly	CGC Arg 190	GTC Val	TAC Tyr	GAG Glu	CTG Leu	GCC Ala 195	GGT Gly	GAA Glu	CCG Pro	GCA Ala	TAT Tyr 200	ACG Thr	3748
CTC Leu	ACC Thr	GAA Glu	CTG Leu 205	GCA Ala	GCT Ala	GAG Glu	GTG Val	GCG Ala 210	CCG Pro	CAA Gln	GCA Ala	GGA Gly	AAG Lys 215	ACC Thr	GTC Val	3796
GTG Val	TAT Tyr	TCG Ser 220	AAC Asn	CTA Leu	TCC Ser	GAG Glu	AGC Ser 225	GAT Asp	TAC Tyr	CGA Arg	TCT Ser	GCG Ala 230	TTG Leu	ATC Ile	AGT Ser	3844
GCG Ala	GGC Gly 235	CTT Leu	CCC Pro	GAT Asp	Gly	TTT Phe 240	GCG Ala	GCA Ala	TTG Leu	CTC Leu	GCA Ala 245	GAC Asp	TCT Ser	GAT Asp	GCA Ala	3892

GGC GCA AGC GGC TAT TTG TTT GAT TCC AGT GGA GAC AGT CGC AAG Gly Ala Ala Lys Gly Tyr Leu Phe Asp Ser Ser Gly Asp Ser Arg Lys 250 260 265	3940
CTG ATC GGT CGC CCA ACC ACT CCG ATG TCG GAA GCC ATC GCG GCA GCA Leu Ile Gly Arg Pro Thr Thr Pro Met Ser Glu Ala Ile Ala Ala Ala 270 275 280	3988
ATT GGC CGC TAAAACTGCA TTTTCGCGAC TTGAGTGACA CCTGGGTTAG	4037
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CGCTTGCCCG GCGGCGCCC CGCTATTGGA TGATTCTCAA CTTCCTGGTG CCGGCGTCTT	4157
GTTGGGGCCC AAACAGGCGG GCATAACGCA ATGTGGCATT TGCACTGTCG CGCATGATGG	4217
CTTCTGCTCG AGCACCTTGC CCGCTAATCA GCGCGTCTAC CACAGCATGA TGCTGCATGT	4277
TGGCAAAATT GAACCGGCGG TACTCTTGGG GAGGTTGCTA CCGTCGACGG CCAGTGAACT	4337
GACAGAGGCA AAGGGCAGGT GTTCATTCCG AGCCAATGCT TCACCTATGG CAGCGTTACC	4397
GCTGGCATCC ACGATAGCTT GATGGAAGCG CTTGTTGATG TCGTGGTATT CGGCGAGGTC	4457
GTCTTCGCTG ACATAACCTT TCTCAAATAG GGCATCGCCC TGGGCCAAGC ACTGCAAGAG	4517
GATCTCTTGC GTTTCACTGG ATAGCCCTCG CTCGGCAGCC TGCCTTGCGG CCAGTCCTTC	4577
AAGTACCCCT CGAACCTCCA CCGCGCCTGC CAGGTCATTT GGGGTCATTT GCCGCACTGC	4637
ATAGCCACGT GCGCCTTGGC GATCAGTAAC CCTTCCTGTT CTAGCGCTCG GAACGCAATG	4697
CGGATAGGTG TGCGCCGACA CTCCCAGGCG CTCGGCAGTG GGGATTTCGG CGATGCGCTC	4757
TCCTGCCGGG AGTTCGCCAT CCACAATCAT TTTGCGCAGT AGATTGAGTA CTCGCTGCCC	4817
GGGCCCGCTC ATTTCAGCCT CCGATTGGAT CCAGTAATGG TTTGAGAGAA TTTTACTCGC	4877
AAGGGATTTC TGGGCAATAG CCCCGCTGAT TGCTGGTTTT TGTATGTGGC GTGCGACTAT	4937
CGCACAGAAT TGGATCCACC TTGGCGCAAA AAAACTGGAG CTACCTCATC GGTCGTGGTT	4997
ATATTGGATC CCATAAGGTC AAGTTCATAG CTGATTTTGG CTTTAGATGT CCATTGTGGA	5057
TCCAAAAACA AGATCGCCAT TGAGGAACGC GCCATGTTTC CGAAAAACGC CTGGTATGTC	5117
SCTTGCACTC CGGATGAAAT CGCAGATAAG CCGCTAGGCC GTCAGATCTG CAACGAAAAG	5177
ATTGTCTTCT ATCGGGGGCC GGAAGGACGT GTTGCCGCGG TAGAGGATTT CTGCCCTCAT	5237
CGCGGGGCAC CGTTGTCCCT GGGTTTCGTT CGCGACGGTA AGCTGATTTG CGGCTACCAC	5297

GGTTTGGAAA TGGGCTGCGA GGGCAAAACG CTCGCGATGC CCGGGCAGCG CGTTCAAGGC 5357 TTCCCTTGCA TCAAAAGCTA CGCGGTAGAA GAGCGATACG GCTTTATCTG GGTATGGCCT 5417 GGTGATCGCG AGCTGGCGGA TCCGGCGCTT ATTCACCACC TGGAGTGGGC CGATAATCCG 5477 GAGTGGGCCT ATGGTGGCGG TCTCTACCAC ATCGCTTGTG ATTACCGCCT GATGATCGAC 5537 ARCCTCATGG ATCTCACCCA TGAGACCTAT GTGCATGCCT CCAGCATCGG TCAAAAGGAA 5597 ATTGACGAGG CACCGGTCAG TACTCGTGTC GAGGGCGACA CCGTGATTAC CAGCCGGTAC 5657 ATGGATAACG TCATGGCCCC TCCGTTCTGG CGTGCTGCGC TTCGTGGCAA CGGCTTGGCC 5717 GACGATGTAC CGGTTGATCG CTGGCAGATC TGCCGATTCG CTCCTCCGAG TCACGTACTG 5777 ATCGAAGTAG GTGTGGCTCA TGCGGGCAAA GGCGGATATG ACGCGCCGGC GGAATACAAG 5837 GCCGGCAGCA TAGTGGTCGA CTTCATCACG CCGGAGAGTG ATACCTCGAT TTGGTACTTC 5897 TGGGGCATGG CTCGCAACTT CCGTCCGCAG GGCACGGAGC TGACTGAAAC CATTCGTGTT 5957 GGTCAGGGCA AGATTTTTGC CGAGGACCTG GACATGCTGG AGCAGCAGCA GCGCAATCTG 6017 CTGGCCTACC CGGAGCGCCA GTTGCTCAAG CTGAATATCG ATGCCGGCGG GGTTCAGTCA 6077 CGGCGCGTCA TTGATCGGAT TCTCGCAGCT GAACAAGAGG CCGCAGACGC AGCGCTGATC 6137 GCGAGAAGTG CATCATGATT GAGGTAATCA TTTCGGCGAT GCGCTTGGTT GCTCAGGACA 6197 TCATTAGCCT TGAGTTTGTC CGGGCTGACG GTGGCTTGCT TCCGCCTGTC GAGGCCGGCG 6257 CCCACGTCGA TGTGCATCTT CCTGGCGGCC TGATTCGGCA GTACTCGCTC TGGAATCAAC 6317 CAGGGGCGCA GAGCCATTAC TGCATCGGTG TTCTGAAGGA CCCGGCGTCT CGTGGTGGTT 6377 CGAAGGCGGT GCACGAGAAT CTTCGCGTCG GGATGCGCGT GCAAATTAGC GAGCCGAGGA 6437 ACCTATTCCC ATTGGAAGAG GGGGTGGAGC GGAGTCTGCT GTTCGCGGGC GGGATTGGCA 6497 TTACGCCGAT TCTGTGTATG GCTCAAGAAT TAGCAGCACG CGAGCAAGAT TTCGAGTTGC 6557 ATTATTGCGC GCGTTCGACC GACCGAGCGG CGTTCGTTGA ATGGCTTAAG GTTTGCGACT 6617 TTGCTGATCA CGTACGTTTC CACTTTGACA ATGGCCCGGA TCAGCAAAAA CTGAATGCCG 6677 CAGCGCTGCT AGCGGCCGAG GCCGAAGGTA CCCACCTTTA TGTCTGTGGG CCCGGCGGGT 6737 TCATGGGGCA TGTGCTTGAT ACCGCGAAGG AGCAGGGCTG GGCTGACAAT CGACTGCATC 6797 GAGAGTATTT CGCCGCGGCG CCGAATGTGA GTGCTGACGA TGGCAGTTTC GAGGTGCGGA 6857 TTCACAGCAC CGGACAAGTG CTTCAGGTCC CCGCGGATCA AACGGTCTCC CAGGTGCTCG 6917 ATGCGGCCGG AATTATCGTT CCCGTTTCTT GTGAGCAGGG CATCTGCGGT ACTTGCATCA 6977

CTCGGGTGGT AGACGGAGAG CCTGATCATC GTGACTTCTT CCTCACGGAT GCGGAGAAGG 7037 CAAAGAACGA CCAGTTCACC CCCTGTTGCT CGCGAGCCAA GAGCGCCTGT TTGGTCTTGG 7097 ATCTCTAACT CATCCCCGTG TCCGGTCCCC TGCTTTGGTG CGGCGGACTG TGCGCGGGTA 7157 AGTAAACAGG CTCAACCGTT TTTAGCGGGA TAACCATTCT TGAGGATGAA GGAGGGTTAT 7217 CCCGCTCTTT TCATGCACCA AGCCATTCAT AGTCACCAGC TGCTTCTACG TGCTGCTGCG 7277 TTACAAGTTT ATTCAGAAGG AAATCGGAAT GATCAAATCC CGCGCCGCTG TGGCGTTCGC 7337 ACCCAATCAG CCATTGCAGA TCGTCGAAGT GGACGTGGCT CCGCCCAAGG CCGGTGAAGT 7397 CCTGGTGCGG GTCGTGGCCA CCGGCGTTTG CCACACCGAT GCCTACACCC TGTCCGGCGC 7457 TGATTCCGAG GGCGTTTTCC CCTGCATCCT TGGTCACGAA GGCGGCGGCA TTGTCGAAGC 7517 GGTGGGCGAG GGCGTCACCT CGCTGGCGGT CGGCGACCAC GTGATCCCGC TCTACACGGC 7577 CGAATGCCGT GAGTGCAAGT TCTTCAAGTC CGGCAAGACC AACCTGTGCC AGAAAGTGCG 7637 TGCTACTCAG GGCAAGGGTC TGATGCCGGA CGGCACCTCC CGCTTCAGCT ACAACGGTCA 7697 GCCGATCTAC CACTACATGG GCTGCTCGAC CTTCTCCGAG TACACCGTGC TGCCGGAAAT 7757 CTCCCTGGCG AAGATTCCCA AGAATGCGCC GCTGGAGAAA GTCTGCCTGC TGGGCTGCGG 7817 CGTGACCACC GGCATTGGCG CGGTGCTGAA CACTGCCAAG GTGGAGGAGG GTGCTACCGT 7877 GGCCATCTTC GGCCTGGGCG GCATCGGCTT GGCGGCGATC ATCGGCGCGA AGATGGCCAA 7937 GGCCTCGCGC ATCATCGCCA TCGACATCAA TCCGTCCAAG TTCGATGTGG CTCGCGAGCT 7997 GGGCGCCACT GACTTCGTCA ATCCGAACGA TCACGCGAAG CCGATCCAGG ATGTCATCGT 8057 CGAGATGACT GATGGCGGTG TGGACTACAG CTTCGAGTGC ATCGGCAACG TTCGACTCAT 8117 GCGCGCAGCA CTCGAGTGCT GCCACAAGGG CTGGGGCGAA TCCGTGATCA TCGGCGTGGC 8177 GCCGGCGGGG GCCGAAATCA ACACCCGTCC GTTCCACCTG GTGACCGGTC GCGTCTGGCG 8237 GGGTTCGGCG TTCGGTGGCG TAAAGGGCCG CACCGAACTG CCGAGCTACG TGGAGAAGGC 8297 ACAGCAGGGC GAGATCCCGC TGGACACCTT CATCACTCAC ACCATGGGCC TGGACGACAT 8357 CAACACGGCC TTCGACCTGA TGGACGAAGG GAAGAGCATC CGCTCTGTTG TTCAATTGAG 8417 TCGCTAGTGA AGTGGGGTGA GGAAATTGGA TTAGGAGGCG GATGGTTCCT GCCGCTTAAC 8477 CACCTTGTCC CAGCTTCTGG CTGAGATTTC CAAGATTCGG TGAAATTTGC CATGCCGCAA 8537 ACTCTTGCTG GACGGTTGAG TCTGTTATCC GGCACCGACG AATTAACCCT GCTTCTTCGG 8597

GGTGGTCGGG GCATTGAGCG TGAAGCCTTG CGGGTCGATG TTCAAGGTGA ACTGGCGCTG 8657 ACGCCTCACC CGGCGGCGCT TGGCTCTGCG TTGACCCATC CGACAATTAC TACGGATTAC 8717 GCCGAGGCCC TGCTTGAGTT GATCACTCGG CCGGCAACCG ATTGTGCGCA AGCCTTGGCT 8777 GAGCTGGAGG AGCTTCACCG TTTCGTTCAT TCGAGACTTG AGGGGGAGTA TCTCTGGAAT 8837 CTGTCCATGC CTGGCAGATT GCCGGTTGAT GAGCAAATCC CGATTGCTTG GTATGGACCA 8897 TCAAATCCAG GCATGTTGCG CCACGTTTAT CGCCGTGGCC TAGCTCTGCG TTATGGCAAG 8957 CGAATGCAAT GCATCGCAGG GATTCACTAC AACTACTCAC TGCCGCCAGA GCTTTTCGCT 9017 GTCCTGACCA AGGCAGAGGT CGGGTCTCCC AAGTTACTGG AGCGCCAGTC AGCAGCTTAC 9077 ATGCGCCAAA TTCGCAACCT TCGGCAATAC GGTTGGTTGC TGGCCTACTT GTTCGGCGCT 9137 TCCCCCGCCA TCTGCAAGAG CTTCTTGGGG GGCGAGAGAG ATGAGCTAGC TCGCATGGGG 9197 GGCGATACGC TTTACATGCC CTATGCAACC AGCTTGCGCA TGAGTGACAT CGGGTACCGC 9257 AACCGTGCCA TGGATGATCT ATCTCCCAGC CTGAATGATC TGGGTGCCTA TATTCGCGAT 9317 ATTTGCCGTG CTCTTCACAC TCCCGATGCC CAGTACCAGG CGCTGGGTGT GTTTGCACAG 9377 GGCGAGTGGC GGCAGTTAAA CGCCAATCTA TTGCAGTTGG ATAGTGAGTA CTACGCACTG 9437 GCGCGACCGA AGTCAGCGCC CGAGCGGGGG GAGCGAAACC TGGATGCTCT CGCTAGGCGT 9497 GGAGTCCAGT ATGTGGAGCT GCGCGCACTG GATCTCGATC CATTCTCCCC GTTAGGCATT 9557 GGCCTGACCT GCGCCAAGTT CCTCGATGGC TTTTTGCTTT TCTGCTTGTT GTCTGAGGCG 9617 CCGGTTGATG ATCGAAATGC CCAGCGTTCA AGACCGGGAA AATCTGAGCC TGGCCGGCAA 9677 GTACGGGCGT CACCTGGCTT AAAGCTGCAT CGGAATGGTC AGTCCATTCT CCTCAAGGAT 9737 TGGGCGCAGG AAGTGTTGAC GGAGGTTCAG GCCTGTGTGG AATTGCTCGA CAGTGCAAAT 9797 GGGGGCTCAT CTCACGCATT GGCTTGGTCA GCACAGGAGG AAAAGGTGCT TAATCCGGAT 9857 TGTGCGCCAT CAGCTCAGGT GCTCGCAGAG ATACACAGAC ACGGTGGGAG CTTCACGGCA 9917 TTTGGTCGCC AATTAGCTAT CGACCATGCA AAACACTTCA GTGCCTCCTC GCTTGAGGCT 9977 GGCGTAGCCA AAGCGCTTGA CCTCCAGGCG ACGTCGTCTC TGCGCGAGCA GCATCAATTG 10037 GAGGCCAACG ACCGTGCGCC ATTTTCTGAC TACCTTCAGC AATTCTCCCT GGCTTTCGGT 10097 CAATCCGTCG GCGCCTCTCG TGCGCCCAAC CCTACCGCGC ACCTCATCGA TCTGACCCCT 10157 CCTGTCTAAG GTTGTCGTGG GAGCAGATCC GTGGGCCGAG CTTCCTCCAG GGCCTGGCCG 10217 CAGCGATCCA GTTGCTAGGT CCCTATGCTC TTGCATAGGG TAAAAATTAG TTATTGTGTT 10277

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GGACTGACCG GATTTCATGT GTGCCGGTGA AGTGAAGATG TCTGTGAGTG CAATGGTGGT GGTATTGAAA ATGGGCCGAG GCTGGCCTAT TGTTTAGAAT TTCAAGAATG ACAACTATTC 16997 GGTGGCGGCG TATGTCCATT CACTCTGAGG GGATCACTCT CGCGGATTCG CCGCTGCATT 17057 GGGCGCATAC CCTGAATGGA TCAATGCGTA CTCATTTCGA AGTCCAGCGT CTTGAGCGGG 17117 GTAGAGGTGC CTCCCTTGCC CGATCTAGAT TTGGCGCGGG TGAGCTGTAC AGTGCCATTG 17177 CACCAAGCCA GGTACTTCGC CACTTCAACG ACCAGCGAAA TGCTGATGAG GCTGAGCACA 17237 GCTATTTGAT TCAGATACGA AGTGGCGCTT TGGGCGTTGC ATCCGGCGGA AGAAAGGTGA 17297 TCTTGGCAAA TGGTGATTGC TCCATAGTTG ATAGTCGCCA AGACTTCACA CTTTCCTCGA 17357 ACTCTTCGAC CCAAGGTGTC GTAATACGCT TTCCGGTGAG TTGGCTGGGA GCGTGGGTGT 17417 CCAATCCGGA GGATCTTATC GCCCGACGAG TTGATGCTGA GGTAGGGTGG GGTAGGGCGC 17477 TAAGCGCATC GGTTTCTAAT CTAGATCCAT TGCGCATCGA CGATTTAGGT AGCAATGTAA 17537 ATGGCATTGC AGAGCATGTT GCTATGTTAA TTTCACTAGC AAGTTCTGCG GTTAGTTCTG 17597 AAGATGGGGG TGTGGCTCTT CGGAAAATGA GGGAAGTGAA GAGAGTACTC GAGCAGAGTT 17657 TCGCAGACGC TAATCTCGGG CCGGAAAGTG TTTCAAGTCA ATTAGGAATT TCGAAACGCT 17717 ATTTGCATTA TGTCTTTGCT GCGTGCGGTA CGACCTTTGG TCGCGAGCTG TTGGAAATAC 17777 GCCTGGGCAA AGCTTATCGA ATGCTCTGTG CGGCGAGTGA CTCGGGTGCT GTGCTGAAGG 17837 TGGCCATGTC CTCAGGTTTT TCGGATTCAA GCCATTTCAG CAAGAAATTT AAGGAAAGAT 17897 ACGGTGTTTC GCCTGTCTCC TTGGTGAGGC AGGCTTGATT TCCCATAGCG TTATTGCGGT 17957 CGTCGTTGCA AATGCGGACC TGCGTGATCA TCAAGGCTAA GACTGCCACA TTAGGTGTCG 18017 ACTCGAGCGT CCCTCTATCC GCCTGACCGC GCTCCGTCCC TAGTACCTAG GAAATTGAGT 18077 GGGCCTACTT GCCAGGGCCA GTTGGATTCG GTGCTGGTGA GCGCTGCGGG TGACAGAATC 18137 CTGATCGTGG CGATCACGAT GGCGATAAAG TTGCCCGGTG TCGTAGATCG CAGGGTGACC 18197 AAGACGGGGA CTCATGGCGC GGATCCCGCC AGTGATGCCT TCGCATGACG CCACCTCTCT 18257 CCTCCGCTCA GCCTTCATGC CTGACTAATT AAGTCGTATA TCAATCTGGC TCTGTGCCGC 18317 ATTCAGTTCC TCCAGCTGCA TTGTCTCTCG GCGGGAGGGC ATTCCCCTGC ATTGGCCAAA 18377 TGGGTCCCCT TGTTCACGAC CGGACAAGCG CACCGTGCTG CCCGTTCGTC GTGTGCCCTG 18437 TCAAAAAGCC TGGCGACGAA AGGGCGGCAG GCCGCATGGC CACGGCTGGG CGGTAACTGA 18497

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GAGGCAGATA ATGCCTTTGC GGCAACTGGC CCCGATACGA TTGCCAAGTT CTTGTTCACT 21857 TCTGGCTCTA CCAAACTGCC TAAGGCGGTG CCGACTACTC AGCGAATGCT CTGCGCCAAT 21917 CAGCAGATGC TTCTGCAAAC TTTCCCGGTT TTTGGTGAAG AGCCGCCGGT GCTGGTGGAC 21977 TGGTTGCCGT GGAACCACAC CTTCGGCGGC AGCCACAACA TCGGCATCGT GTTGTACAAC 22037 GGCGGCACGT ACTACCTTGA CGACGGTAAA CCAACCGCCC AAGGGTTCGC CGAGACGCTT 22097 CGCAACTTGA GCGAAATCTC TCCCACTGCG TACCTCACTG TGCCGAAAGG CTGGGAGGAA 22157 TTAGTGGGTG CCCTTGAGCG AGACAGTACC CTGCGCGAAC GCTTCTTCGC TCGCATGAAG 22217 CTGTTCTTCT TCGCGGCGGC TGGGTTGTCG CAAGGGATCT GGGATCGTTT GGACCGGGTC 22277 GCTGAACAGC ACTGTGGTGA GCGCATTCGC ATGATGGCGG GTCTGGGCAT GACGGAGACT 22337 GCTCCTTCCT GCACTTTTAC CACCGGACCG CTGTCGATGG CTGGTTACAT TGGGCTGCCA 22397 GCGCCTGGCT GCGAGGTCAA GCTCGTTCCG GTCGATGGGA AATTGGAAGG GCGTTTCCAT 22457 GGTCCGCACG TCATGAGCGG CTACTGGCGT GCTCCTGAAC AAAATGCCCA AGCGTTCGAC 22517 GAGGAAGGCT ATTACTGCTC CGGTGATGCC ATCAAATTGG CAGATCCTGC CGATCCTCAG 22577 AAAGGTCTGA TGTTTGACGG TCGAATTGCT GAAGACTTCA AGCTGTCCTC AGGGGTATTT 22637 GTCAGCGTTG GGCCATTGCG CACGCGGGCG GTTCTGGAAG GCGGCTCTTA CGTCCTGGAC 22697 GTAGTGGTTG CTGCTCCTGA TCGTGAATGC CTTGGATTGC TCGTGTTTCC GCGTCTTCTC 22757 GACTGCCGTG CCTTGTCGGG GCTAGGAAAA GAGGCGTCGG ACGCCGAGGT GCTTGCCAGT 22817 GAGCCGGTTC GGGCCTGGTT TGCTGACTGG CTCAAACGAC TCAATCGAGA AGCAACTGGC 22877 AATGCCAGTC GCATCATGTG GGTAGGGCTC CTCGATACGC CGCCGTCGAT TGATAAGGGC 22937 GAGGTCACTG ACAAGGGCTC GATCAACCAG CGCGCTGTTT TGCAATGGCG GTCGGCGAAA 22997 GTTGATGCGC TGTATCGTGG TGAAGATCAA TCCATGCTGC GTGACGAGGC CACACTGTGA 23057 GTTGGTCAGG GGGGGCTTAC TCGGCGTTTT CCGACACTGC GTTGGTTGCG GCAGTGCGCA 23117 CCCCCTGGAT TGATTGCGGG GGTGCCCTGT CGCTGGTGTC GCCTATCGAC TTAGGGGTAA 23177 AGGTCGCTCG CGAAGTTCTG ATGCGTGCGT CGCTTGAACC ACAAATGGTC GATAGCGTAC 23237 TCGCAGGCTC TATGGCTCAA GCAAGCTTTG ATGCTTACCT GCTCCCGCGG CACATTGGCT 23297 TGTACAGCGG TGTTCCCAAG TCGGTTCCGG CCTTGGGGGT GCAGCGCATT TGCGGCACAG 23357 GCTTCGAACT GCTTCGGCAG GCCGGCGAGC AGATTTCCCA AGGCGCTGAT CACGTGCTGT 23417 GTGTCGCGGC AGAGTCCATG TCGCGTAACC CCATCGCGTC GTATACACAC CGGGGCGGGT 23477

TCCGCCTCGG TGCGCCCGTT GAGTTCAAGG ATTTTTTGTG GGAGGCATTG TTTGATCCTG 23537 CTCCAGGACT CGACATGATC GCTACCGCAG AAAACCTGGC GCGCCTGTAC GGAATCACCA 23597 GGGGAGAGC TAATTCCTAC GCGGTAAGCA GCTTCGAGCG CGCATTGAGG GCGCAAGAGG 23657 AGARATGGAT TGACCAAGAG ATCGTGGCTG TTACGGATGA ACAGTTCGAT TTAGAGGGCT 23717 ACAACAGTCG AGCAATTGAA CTGCCTCGGA AGGCAAAATT GTTGATCGTG ACAGTCATCC 23777 GCGGCCTAGC AGTCTTTGAA GCCCTTTCCC GATTGAAGCC TGTTCATTCT GGCGGGGTGC 23837 AGACTGCGGG CAACAGCTGT GCCGTAGTGG ACGGCGCCGC GGCGGCTTTG GTGGCTCGAG 23897 AGTCGTCTGC GACACAGCCG GTCTTGGCTA GGATACTGGC TACCTCCGTA GTCGGGATCG 23957 AGCCCGAGCA TATGGGGCTC GGCCCTGCGC CCGCGATTCG CCTGCTGCTT GCGCGTAGTG 24017 ATCTTAGTTT GAGGGATATC GACCTCTTTG AGATAAACGA GGCGCAGGCC GCCCAAGTTC 24077 TAGCGGTACA GCATGAATTG GGTATTGAGC ACTCAAAACT TAATATTTGG GGCGGGGCCA 24137 TTGCACTTGG ACACCCGCTT GCCGCGACCG GATTGCGTCT CTGCATGACC CTCGCTCACC 24197 AATTGCAAGC TAATAACTTT CGATATGGAA TTGCCTCGGC ATGCATTGGT GGGGGACAGG 24257 GGATGGCGGT TCTTTTAGAG AATCCCCACT TCGGTTCGTC CTCTGCACGA AGTTCGATGA 24317 TTAACAGAGT TGACCACTAT CCACTGAGCT AACGGGCATC TCCTTTGTTG CTTTGAGGTG 24377 GCGCACGAAG GAGGGCTCGA AAATCTCTGC TAAAAACAAG AAGAAGGAAC AGGGAACATG 24437 ATTAGTTTCG CTCGTATGGC AGAAAGTTTA GGAGTCCAGG CTAAACTTGC CCTTGCCTTC 24497 GCACTCGTAT TATGTGTCGG GCTGATTGTT ACCGGCACGG GTTTCTACAG TGTACATACC 24557 TTGTCAGGGT TGGTGGAAAA GAGCGCGATA GCTGGTGAGT TGCGGGCGAA AATTCAGGAA 24617 CTGAAGGTTC TGGAGCAGCG CGCCTTATTC ATCGCCGATG AAGGGTCGCT GAAGCAGCGC 24677 TCGATCCTCC TAAGTCAGGT GATAGCTGAA GTTAATGATG CTATAGATAT TTTTGACTTT 24737 CAGCGCGGAC GATCTGAGTT ACTTAAATTC GCTGCTTCTT CGCGCGAAGC AAGTTACTCC 24797 ATTGAGGTCG GTAGTAACGC TGCGGCCGAT AAGTTGCAGT CGGGCGAACC AAGTGACGCA 24857 TTGATGGTTG CCGATAAAAA GCTGAATGTT GAGTATGAGC AATTGAGTTC TGCTGTGAAT 24917 GCACTGATGG GGCATTTAAT TGAGGATCAG AATGAAAAAG TTCCACTAAT CTACTATATG 24977 CTTGGCGGCG TAACTTTGTT TACGATGCTC ATGAGTGCTT ATTCGGTCTG GTTCATTTCG 25037 CGTCAGTTAG TTCCGCCATT AAAGTCGACG GTGCAGCTTG CCGAGCGGAT TGCATCAGGC 25097

GACTTGGCTG ATGTCGGGGA CAGCAGGCGC AAGGATGAAA TCGGTCAGTT GCAAAGTGCA 25157 ACTAGGCGGA TGGCGATTGG ACTGCGTAAT CTGGTCGGTG ATATTGGTCA AAGTCGTGCG 25217 CARCTGGTTT CATCGTCCAG CGACCTTTCG GCCATCTGTG CTCAGGCTCA GATTGATGTC 25277 GAGTGCCAGA AGCTTTCGGT CGCCCAGGTC TCTACCGCCG TGAACGAGTT GGTTGAAACC 25337 GTCCAGGCAA TAGCAAAAAG CACCGAAGAG GCAGCAACAG TCGCCGTCTT GGCCGATGAA 25397 AAGGCACGCG GTGGTGAAAG TGTCGTTAAC AAGGCCGTTG ATTTCATTGA GCACCTCTCC 25457 GGAGATATGG CGGAACTGGG AGACGCAATG GAGCGGCTTC AGAACGACAG TGCGCAGATC 25517 AATAAGGTAG TAGACGTCAT TAAGGCTGTG GCGGAGCAGA CCAATCTGCT AGCCCTGAAT 25577 25637 GAGGTTCGTG CTTTGGCGAT GCGCACCCAA CAATCGACCA AAGAAATTGA GAGGCTAGTG 25697 GTTTCATTGC AGCAGGGAAG TGAAGCTGCG GGCGAGTTGA TGCGGCGTGG CAAGGTCCGG 25757 ACGCATGACG TCGTTGGATT GGCCCAGCAA GCCGCGCGCC GCGCTACTCG AAATTACCCA 25817 GCTGTCGCCG GCATCCAAGC GATGAACTAT CAGATCGCCG CTGGAGCAGA GCAGCAAGGG 25877 GCTGCTGTGG TTCAAATCAA CCAGAATATG CTTGAAGTGC ATAAGATGGC TGACGAGTCC 25937 GCCATTAAAG CGGGACAGAC CATGAAGTCA TCGAAGGAGC TTGCTCACCT CGGCAGTGCG 25997 CTACAAAAAT CCGTTGATCG ATTCCAGCTG TAGCGCTCCG GGTGGCTGAA ACGCGCATTT 26057 TCGTTAAGGT CTTCAGCGCG GTCTGCTGGT GCGTGGGCCG CTAGCCTAAC TGTTGCGCTT 26117 CAGGCTCCGC ATGGATCTTG TGCAGCAGCA ATAGCAATTG TTCACGTTCG TCATCACTCA 26177 GCATCGACGT CGCGTCTTGG TCGCTCTGTA CCACGATCTT CTTCAGCTCT TTGAGCTGCG 26237 TCTCCCCAGC TTTGCTGAGA AATATCCCAT AGGAACGCTT GTCCGGCTTG CAGCGCACGC 26297 GCACAGCAAG GCCGAGCTTC TCGAGCTTGT TCAGCAAGGG AACCAGTTGT GGTGGTTCGA 26357 TTGCGAGCAT CCGCGCTAGG TCAGCCTGCA TAAGCCCAGG GCTCGCTTCG ATGATTAGAA 26417 GTGCCGACAG CTGCGCCGGG CGTAGGTCAT ATGGCGTCAG GGCTTCAATC AGGCCCTGAG 26477 CGAGCTTCAG CTGTGAGCCG GCGTAAGGCA TAGCCAATCA ATTGATTCAG GAGCGTATCG 26537 CCCGGTTCTA TCAGCGGGCC GCTTTCGAAA GTCATGGTGT TAGCCGGTAG GGTCTTTTTC 26597 TTGGCCATGC TTGTTGCCTG AACCTTCGTT GACATAGGGC AGAGGTGCGT TTGCCGCTTC 26657 GCTTCGCGAT GAACCGCATC GAGATGCTGA GGTCAGGATT TTTCCTTAAC TCGCGTAAGC 26717 ATTCTGTCAT TTTTTTGGTG GCTTTGAACA GCCTGATGAA AGGTGGTCTC GCCCTTTGAG 26777

GCCGATTCTT GGGCGCTTGG CGGCGTCGAA GCGATGCTCC ACTACCGATT AAGATAATTA 26837 AAATAAGGAA ACCGCATGGT TTCTTATGTG AATTTGTCTG GCATACTCCA GCTCAAGGGC 26897 AATTTTTGGG CTATTGGCTG AGCAGTTGCC TCTATATGGT TATTCAGAAT AACAATTGAC 26957 TCCTCAGGAG GTCAGCGATG AGCATTCTTG GTTTGAATGG TGCCCCGGTC GGAGCTGAGC 27017 AGCTGGGCTC GGCTCTTGAT CGCATGAAGA AGGCGCACCT GGAGCAGGGG CCTGCAAACT 27077 TGGAGCTGCG TCTGAGTAGG CTGGATCGTG CGATTGCAAT GCTTCTGGAA AATCGTGAAG 27137 CAATTGCCGA CGCGGTTTCT GCTGACTTTG GCAATCGCAG CCGTGAGCAA ACACTGCTTT 27197 GCGACATTGC TGGCTCGGTG GCAAGCCTGA AGGATAGCCG CGAGCACGTG GCCAAATGGA 27257 TGGAGCCCGA ACATCACAAG GCGATGTTTC CAGGGGCGGA GGCACGCGTT GAGTTTCAGC 27317 CGCTGGGTGT CGTTGGGGTC ATTAGTCCCT GGAACTTCCC TATCGTACTG GCCTTTGGGC 27377 CGCTGGCCGG CATATTCGCA GCAGGTAATC GCGCCATGCT CAAGCCGTCC GAGCTTACCC 27437 CGCGGACTTC TGCCCTGCTT GCGGAGCTAA TTGCTCGTTA CTTCGATGAA ACTGAGCTGA 27497 CTACAGTGCT GGGCGACGCT GAAGTCGGTG CGCTGTTCAG TGCTCAGCCT TTCGATCATC 27557 TGATCTTCAC CGGCGGCACT GCCGTGGCCA AGCACATCAT GCGTGCCGCG GCGGATAACC 27617 TAGTGCCCGT TACCCTGGAA TTGGGTGGCA AATCGCCGGT GATCGTTTCC CGCAGTGCAG 27677 ATATGCCGGA CGTTGCACAA CGGGTGTTGA CGGTGAAAAC CTTCAATGCC GGGCAAATCT 27737 GTCTGGCACC GGACTATGTG CTGCTGCCGG AAGAATCGCT GGATAGCTTT GTCGCCGAGG 27797 CGACGCGCTT CGTGGCCGCA ATGTATCCCT CGCTTCTAGA TAATCCGGAT TACACGTCGA 27857 TCATCAATGC CCGAAATTTC GACCGTCTGC ATCGCTACCT GACTGATGCG CAGGCAAAGG 27917 27977 GAGGGCGCGT CATTGAAATC AATCCTGCGG CCGAAGAGTT GGGGGATAGT GGTATCAGGA AGATCGCGCC CACTITGATC GIGAATGTGT CGGATGAAAT GCTGGTCTTG AACGAGGAGA 28037 TCTTTGGTCC GCTGCTCCCG ATCAAGACTT ATCGTGATTT CGACTCGGCT ATCGACTACG 28097 TCAACAGCAA GCAGCGACCA CTTGCCTCGT ACTTCTTCGG CGAAGATGCG GTTGAGCGTG 28157 AGCAAGTGCT TAAGCGTACG GTTTCGGGCG CCGTGGTCGT GAACGATGTC ATGAGCCATG 28217 TGATGATGGA TACGCTTCCA TTTGGTGGTG TGGGGCACTC GGGGATGGGG GCATATCACG 28277 GCATTTATGG TTTCCGAACC TTCAGCCATG CCAAGCCTGT TCTCGTGCAA AGTCCTGTGG 28337 GTGAGTCGAA CTTGGCGATG CGCGCACCCT ACGGAGAAGC GATCCACGGA CTGCTCTCTG 28397 TCCTCCTTTC AACGGAGTGT TAGAACCGTT GGTAGTGGTT TTGGACGGGC CCAGGAGCAT 28457 GCGCTTCTGG GCCCGTTTCT TGAGTATTCA TTGGATAGTC ACGCGTGGTA GCTTCGAGCC 28517 TGCACAGCTG ATGAGCACCC TGGAAGGCGC GCTGTACGCG GACGACTGGG TTCATCTTCG 28577 CCATTCATGA CGGAACTCCG TTCCCCAGTA CCGCGATGAC TATTTTGCCT CTTCCGATGT 28637 CCGATTCCAC GCCGCCTGAC GCTAAGCGGG GGCGGGGGCG CCCGCATCCC AGCCCAGACA 28697 GCAACAAATG AGTAGGCTCT TGGATGCCGC GGCGGCTGAG ATTGGTAACG GCAATTTCGT 28757 CAATGTGACG ATGGATTCGA TTGCCCGTGC TGCCGGCGTC TCAAAAAAAA CGCTGTACGT 28817 CTTGGTGGCG AGCAAGGAAG AACTCATTTC CCGGTTAGTG GCTCGAGACA TGTCCAACCT 28877 TGAGCTGCTG CTTTGTCACG AGGTTGAGTC TGCGGAGGCC CTTCAGGATG AGTTGCGAAA 28937 CTATCTGCTG CTCTGGGCGC GCTTGACCTT GTCCCCTCTT GCTTTGGGCA TTTTTCTGAT 28997 GGCCGTGCAG GGGCGTGAAA GTGCCCCGGG CCTGGCGAGA ATCTGGTATC GAGAGGGGGC 29057 AGAGCGTTGC CTCAGCTTGC TTCGGGGATG GTTGGCAAGG ATGGCAAGCC GGGAGCTGAT 29117 CGCTCCTGGA GATATCGACT CCGCAGTGGA GCTTATCGAT TCGCTCCTGA TCTCACAGCC 29177 TTTGAAATTA TTTGGCCTGG GGATCCAGAG CGGCTGGACC GATGATCAGA TCAATCAACG 29237 GGTCACAATC GCTCTCGATG CATTCCGTCG GTGCTATGTC GTTTAGCACC GTTCTCGCGG 29297 GCTGTGGCGG CGTGACCTAT TTGTCTAGTG GTCGGCGCGA AATTCGATAA GAAAGCTGGG 29357 CGCGAGTGAG GCCGAGCCGG CGGGCAGCTT CCGAGACATT GCCTTTCACC TGGCCCAGAG 29417 CATGGCTAAT CATCGCGTCC TCCACTTCTT GCAGCGTCAT CGCGCTCAGG TCCTTTGAGT 29477 CAAGCGGCGA GTCGATTGTG CTGGTCGGTT TGGAGAAGGA AGTACTTGGG CTGCCAGTTT 29537 CCTGTGGCTG ATTATCTTGA GCGGTGGCCA GGATGCCGCT GGCCCCAATG GAGAACATCG 29597 GTTGAGTCAG TCGTTCACCG CTAGTGAAGA GGTGGCTCAC GTCAATGGCT CCATCCTCCG 29657 GAGCGCTGAT GACTCCGCGC TCCACCAAAT TTTGAAGCTC CCGGATGTTT CCTGGAAAGT 29717 CGTAGCCAAG CAGGGCATTG GCTGCACGTG GAGTGAATCC GCTGACCACC CGGCTATGAC 29777 GCTGATTGAA GCGGTGCAGG AAATAGGTCA TCAGGAGGGG AATGTCTTCC TTCCTCTCTC 29837 GAAGCGGCGG GAGGTGGATC GGGTAAACAT TGAGGCGGAA AAAAAGGTCC TCGCGGAACT 29897 CGCCGCGCTG GACGCCTGCG CGAAGATCGA CATTGGTTGC GGCTACCACA CGGACGTCAA 29957 CCTTGAGTGT CCTGCTTCCG CCAACCCGTT CGACCTCCGA CTCTTGCAGG GCGCGAAGTA 30017 ACTTCCCTTG GGCCACGAGG CTTAGCGTCC CTATCTCGTC AAGGAATAGT GTGCCGCCCG 30077

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CTGGGTCTAA	AGTATCTGAC	CGAGGCAGTC	CTGTCGCGCA	TTCAACCCGG	TGGTTCGATT	31757
STCAACGTGT	CCTCTGTGCT	TGGCGCCGAG	TGGCCGGCCC	GCCTTCAGTT	GCATAAGGAG	31817
CTGGGGAGTG	TTGTTGGATT	CTCCGAAGGC	CAGGCATGGC	TTAAGCAGAA	TCCAGTGGCC	31877
CCCGAATTCT	GCTACCAGTA	TTTCAAAGAA	GCACTGATCG	TTTGGTCTCA	AGTTCAGGCG	31937
CAGGAATGGT	TCATGAGGAC	GTCTGTACGC	ATGAACTGCA	TCGCCCCCGG	CCCTGTATTC	31997
ACTCCCATTC	TCAATGAGTT	CGTCACCATG	CTGGGTCAAG	AGCGGACTCA	GGCGGACGCT	32057
CATCGTATTA	AGCGCCCAGC	ATATGCCGAT	GAAGTGGCCG	CGGTGATTGC	ATTCATGTGT	32117
GCTGAGGAGT	CACGTTGGAT	CAACGGCATA	AATATTCCAG	TGGACGGAGG	TTTGGCATCG	32177
ACCTACGTGT	AAGTTCGTGG	ACGCCCTTTG	CACGCGCACT	ATATCTCTAT	GCAGCAGCTG	32237
AAAGCAGCTT	TGGTTTTGAT	CGGAGGTAGC	GGGCGGAAAG	GTGCAGAATG	TCTAAATAAT	32297
AAAGGATTCT	TGTGAAGCTT	TAGTTGTCCG	TAAACGAAAA	TAAAAATAAA	GAGGAATGAT	32357
ATGAAAGCAA	GTAGATCAGT	CTGCACTTTC	AAAATAGCTA	CCCTGGCAGG	CGCCATTTAT	32417
SCAGCGCTGC	CAATGTCAGC	TGCAAACTCG	ATGCAGCTGG	ATGTAGGTAG	CTCGGATTGG	32477
ACGGTGCGTT	GGGGACAACA	CCCTCAAGTA	TAGCCTTGCC	TCTCGCCTGA	ATGAGCAAGA	32537
CTCAAGTCTG	ACAAATGCGC	CGACTGTCAA	TGGTTATATC	CGGATATTCA	AAGTCAGGGT	32597
GATCGTAACT	TTGACCGGGG	GCTTGGTATC	CAATCGTCTC	GATATTCTGT	CGGAGCTTGA	32657
GTCAGTCGT	GACTGGTTGG	TG				32679

- (2) INFORMATION FOR SEQ ID NO: 2:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 284 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Met Ile Ala Ile Thr Gly Ala Ser Gly Gln Leu Gly Arg Leu Thr Ile $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Glu Ala Leu Leu Lys Arg Leu Pro Ala Ser Glu Ile Ile Ala Leu Val 20 25 30

Arg Asp Pro Asn Lys Ala Gly Asp Leu Thr Ala Arg Gly Ile Val Val \$35\$

- Arg Gln Ala Asp Tyr Asn Arg Pro Glu Thr Leu His Arg Ala Leu Ile 50 60
- Gly Val Asn Arg Leu Leu Ile Ser Ser Ser Glu Val Gly Gln Arg 65 70 75 80
- Thr Ala Gln His Arg Ala Val Ile Asp Ala Ala Lys Gln Glu Gly Ile 85 90 95
- Glu Leu Leu Ala Tyr Thr Ser Leu Leu His Ala Asp Lys Ser Ala Leu 100 105 110
- Gly Leu Ala Thr Glu His Arg Asp Thr Glu Gln Ala Leu Thr Glu Ser 115 \$120\$ 125
- Gly Ile Pro His Val Leu Leu Arg Asn Gly Trp Tyr His Glu Asn Tyr 130 \$135\$ 140
- Thr Ala Gly Ile Pro Val Ala Leu Val His Gly Val Leu Leu Gly Cys 145 \$150\$
- Ala Gln Asp Gly Leu Ile Ala Ser Ala Ala Arg Ala Asp Tyr Ala Glu 165 170 175
- Ala Ala Ala Val Leu Thr Gly Glu Asn Gln Ala Gly Arg Val Tyr 180 185 190
- Glu Leu Ala Gly Glu Pro Ala Tyr Thr Leu Thr Glu Leu Ala Ala Glu 195 200 205
 - Val Ala Pro Gln Ala Gly Lys Thr Val Val Tyr Ser Asn Leu Ser Glu 210 215 220
- Ser Asp Tyr Arg Ser Ala Leu Ile Ser Ala Gly Leu Pro Asp Gly Phe 225 230 235
- Ala Ala Leu Leu Ala Asp Ser Asp Ala Gly Ala Ala Lys Gly Tyr Leu 245 250 255
- Phe Asp Ser Ser Gly Asp Ser Arg Lys Leu Ile Gly Arg Pro Thr Thr \$260\$
- Pro Met Ser Glu Ala Ile Ala Ala Ala Ile Gly Arg 275 280
- (2) INFORMATION FOR SEQ ID NO: 3:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1065 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(ix) FEATURE:

- (A) NAME/KEY: CDS
 - (B) LOCATION: 1..1062
 - (D) OTHER INFORMATION:/product=

"Vanillinsaeure-O-Demethylase" /gene= "vanA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

435

	(X1)	SEG	OFM	E DE	SCK.	(PT1C	JIN: 2	PEQ 1	LD NO	J: 3:	i			
											ACT Thr			48
											GAA Glu			96
											GAG Glu			144
											CGC Arg			192
											GAG Glu 360			240
											TGC Cys			288
											TGG Trp			336
											GAG Glu			384
											ATC Ile			432
											CAT			480

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465

450

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864

912

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1008

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635

Leu Ala Ala Glu Gln Glu Ala Ala Asp Ala Ala Leu Ile Ala Arg Ser

630

625

GCA TCA TGA

Ala Ser

CAT GCC TCC AGC ATC GGT CAA AAG GAA ATT GAC GAG GCA CCG GTC AGT

His Ala Ser Ser Ile Gly Gln Lys Glu Ile Asp Glu Ala Pro Val Ser

ACT CGT GTC GAG GGC GAC ACC GTG ATT ACC AGC CGG TAC ATG GAT AAC

Thr Arg Val Glu Gly Asp Thr Val Ile Thr Ser Arg Tyr Met Asp Asn

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(2) INFORMATION FOR SEQ ID NO: 4:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 354 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

Met Phe Pro Lys Asn Ala Trp Tyr Val Ala Cys Thr Pro Asp Glu Ile 1 $$\rm 10$$

Ala Asp Lys Pro Leu Gly Arg Gln Ile Cys Asn Glu Lys Ile Val Phe \$20\$

Tyr Arg Gly Pro Glu Gly Arg Val Ala Ala Val Glu Asp Phe Cys Pro 35 40 45

His Arg Gly Ala Pro Leu Ser Leu Gly Phe Val Arg Asp Gly Lys Leu $50 \hspace{1cm} 55 \hspace{1cm} 60 \hspace{1cm}$

Ile Cys Gly Tyr His Gly Leu Glu Met Gly Cys Glu Gly Lys Thr Leu 65 70 75 80

Ala Met Pro Gly Gln Arg Val Gln Gly Phe Pro Cys Ile Lys Ser Tyr \$85\$ 90 95

Ala Val Glu Glu Arg Tyr Gly Phe Ile Trp Val Trp Pro Gly Asp Arg

Glu Leu Ala Asp Pro Ala Leu Ile His His Leu Glu Trp Ala Asp Asn 115 120 125

Pro Glu Trp Ala Tyr Gly Gly Gly Leu Tyr His Ile Ala Cys Asp Tyr 130 140

Arg Leu Met Ile Asp Asn Leu Met Asp Leu Thr His Glu Thr Tyr Val 145 \$150\$

His Ala Ser Ser Ile Gly Gln Lys Glu Ile Asp Glu Ala Pro Val Ser 165 170 175

Thr Arg Val Glu Gly Asp Thr Val Ile Thr Ser Arg Tyr Met Asp Asn 180 185 190

Val Met Ala Pro Pro Phe Trp Arg Ala Ala Leu Arg Gly Asn Gly Leu 195 200 205

Ala Asp Asp Val Pro Val Asp Arg Trp Gln Ile Cys Arg Phe Ala Pro 210 215 220

Pro Ser His Val Leu Ile Glu Val Gly Val Ala Hıs Ala Gly Lys Gly 225 230230235235

Gly Tyr Asp Ala Pro Ala Glu Tyr Lys Ala Gly Ser Ile Val Val Asp 245 250

Phe Ile Thr Pro Glu Ser Asp Thr Ser Ile Trp Tyr Phe Trp Gly Met 265

Ala Arg Asn Phe Arg Pro Gln Gly Thr Glu Leu Thr Glu Thr Ile Arg 280

Val Gly Gln Gly Lys Ile Phe Ala Glu Asp Leu Asp Met Leu Glu Gln 290

Gln Gln Arg Asn Leu Leu Ala Tyr Pro Glu Arg Gln Leu Leu Lys Leu 310 315

Asn Ile Asp Ala Gly Gly Val Gln Ser Arg Arg Val Ile Asp Arg Ile 325 330

Leu Ala Ala Glu Glu Glu Ala Ala Asp Ala Ala Leu Ile Ala Arg Ser 340 345

Ala Ser

- (2) INFORMATION FOR SEQ ID NO: 5:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 954 base pairs
 - (B) TYPE: nucleic acid

 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..951
 - (D) OTHER INFORMATION:/product= "Vanillin-O-Demethylase" /gene= "vanB"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

ATG ATT GAG GTA ATC ATT TCG GCG ATG CGC TTG GTT GCT CAG GAC ATC Met Ile Glu Val Ile Ile Ser Ala Met Arg Leu Val Ala Gln Asp Ile 355 360

ATT AGC CTT GAG TTT GTC CGG GCT GAC GGT GGC TTG CTT CCG CCT GTC Ile Ser Leu Glu Phe Val Arg Ala Asp Gly Gly Leu Leu Pro Pro Val 375

GCC Ala								144
TAC Tyr								192
GTT Val 420								240
AAT Asn								288
TTC Phe								336
ATT								384
GAG Glu								432
GCG Ala 500								480
TTC Phe								528
CTG Leu								576
GGC Gly								624
GCT Ala								672
AGT Ser 580								720

	GTG Val															768
	GCC Ala															816
	TGC Cys															864
	CTC Leu															912
	TCG Ser 660												TAA			954
(2)	INF	AMAC	TTON	FOR	SEO	1 GT	vo: 1	ñ:								
		() ()	SEQUE A) LE B) T'	ENGTI PE: OPOLO	H: 31 amir OGY:	17 ar no ac line	mino cid ear									
			DAENG					SEQ :	ED NO	o: 6:	:					
Met 1	Ile	Glu	Val	Ile 5	Ile	ser	Ala	Met	Arg 10	Leu	Val	Ala	Gln	Asp 15	Ile	
Ile	Ser	Leu	Glu 20	Phe	Val	Arg	Ala	Asp 25	Gly	Gly	Leu	Leu	Pro 30	Pro	Val	
Glu	Ala	Gly 35	Ala	His	Val	Asp	Val 40	His	Leu	Pro	Gly	Gly 45	Leu	Ile	Arg	
Gln	Tyr 50	Ser	Leu	Trp	Asn	Gln 55	Pro	Gly	Ala	Gln	Ser 60	His	Tyr	Cys	Ile	
Gly 65	Val	Leu	Lys	Asp	Pro 70	Ala	Ser	Arg	Gly	Gly 75	Ser	Lys	Ala	Val	His 80	
Glu	Asn	Leu	Arg	Val 85	Gly	Met	Arg	Val	Gln 90	Ile	Ser	Glu	Pro	Arg 95	Asn	
Leu	Phe	Pro	Leu 100	Glu	Glu	Gly	Val	Glu 105	Arg	Ser	Leu	Leu	Phe 110	Ala	Gly	
Gly	lle	Gly 115	Ile	Thr	Pro	Ile	Leu 120	Cys	Met	Ala	Gln	Glu 125	Leu	Ala	Ala	

- Arg Glu Gln Asp Phe Glu Leu His Tyr Cys Ala Arg Ser Thr Asp Arg $130 \\ 135 \\ 140$
- Ala Ala Phe Val Glu Trp Leu Lys Val Cys Asp Phe Ala Asp His Val 145 \$150\$
- Arg Phe His Phe Asp Asn Gly Pro Asp Gln Gln Lys Leu Asn Ala Ala 165 \$170\$
- Ala Leu Leu Ala Ala Glu Ala Glu Gly Thr His Leu Tyr Val Cys Gly 180 185 190
- Pro Gly Gly Phe Met Gly His Val Leu Asp Thr Ala Lys Glu Gln Gly 195 \$200\$
- Trp Ala Asp Asn Arg Leu His Arg Glu Tyr Phe Ala Ala Ala Pro Asn 210 \$215\$
- Val Ser Ala Asp Asp Gly Ser Phe Glu Val Arg Ile His Ser Thr Gly 225 230 235
- Gln Val Leu Gln Val Pro Ala Asp Gln Thr Val Ser Gln Val Leu Asp 250 \$255\$
- Ala Ala Gly Ile Ile Val Pro Val Ser Cys Glu Gln Gly Ile Cys Gly 260 265 270
- Thr Cys Ile Thr Arg Val Val Asp Gly Glu Pro Asp His Arg Asp Phe 275 280 285
- Phe Leu Thr Asp Ala Glu Lys Ala Lys Asn Asp Gln Phe Thr Pro Cys $290 \hspace{1cm} 295 \hspace{1cm} 300 \hspace{1cm}$
- Cys Ser Arg Ala Lys Ser Ala Cys Leu Val Leu Asp Leu 305 $$\rm 310$$ $$\rm 315$$
- (2) INFORMATION FOR SEQ ID NO: 7:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1119 base pairs (B) TYPE: nucleic acid
 - B) TIFE. NUCTETO ACTO
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1..1116
- (D) OTHER INFORMATION:/product=
 "Formaldehyd-Dehydrogenase"
 /gene= "fdh"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

	(xi	SE	QUEN	CE DI	ESCR:	IPTIC	ON: S	SEQ :	ED NO	o: 7:				
								GCG Ala						48
								CCG Pro						96
								TGC Cys						144
								TTC Phe						192
								GGC Gly 390				 		240
								TAC Tyr						288
								AAC Asn						336
								GAC Asp						384
								ATG Met						432
								CTG Leu 470						480
								GGC Gly						528

				ACT Thr							576
				GGC Gly 515							624
				CGC Arg							672
				GAG Glu							720
				ATC Ile							768
				TTC Phe			-				816
				TGC Cys 595							864
				GGG Gly							912
				TGG Trp							960
				AGC Ser						1	.008
				ATC Ile						1	.056
				ATG Met 675						1	.104
	AGT Ser	CGC Arg	TAG							1	.119

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(2) INFORMATION FOR SEQ ID NO: 8:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 372 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:
- Met Ile Lys Ser Arg Ala Ala Val Ala Phe Ala Pro Asn Gln Pro Leu $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15$
- Gln Ile Val Glu Val Asp Val Ala Pro Pro Lys Ala Gly Glu Val Leu 20 25 30
- Val Arg Val Val Ala Thr Gly Val Cys His Thr Asp Ala Tyr Thr Leu 35 40
- Ser Gly Ala Asp Ser Glu Gly Val Phe Pro Cys Ile Leu Gly His Glu 50 60
- Val Gly Asp His Val Ile Pro Leu Tyr Thr Ala Glu Cys Arg Glu Cys $85 \hspace{1cm} 90 \hspace{1cm} 95$
- Lys Phe Phe Lys Ser Gly Lys Thr Asn Leu Cys Gln Lys Val Arg Ala 100 105 110
- Thr Gln Gly Lys Gly Leu Met Pro Asp Gly Thr Ser Arg Phe Ser Tyr 115 120 125
- As GGly Gln Pro Ile Tyr His Tyr Met Gly Cys Ser Thr Phe Ser Glu 130 $$135\$
- Tyr Thr Val Leu Pro Glu Ile Ser Leu Ala Lys Ile Pro Lys Asn Ala 145 150 155 160
- Fro Leu Glu Lys Val Cys Leu Leu Gly Cys Gly Val Thr Thr Gly Ile 165 \$170\$
- Gly Ala Val Leu Asn Thr Ala Lys Val Glu Glu Gly Ala Thr Val Ala 180 185 190
- Ile Phe Gly Leu Gly Gly Ile Gly Leu Ala Ala Ile Ile Gly Ala Lys 195 200 205
- Met Ala Lys Ala Ser Arg Ile Ile Ala Ile Asp Ile Asn Pro Ser Lys 210 215 220
- Phe Asp Val Ala Arg Glu Leu Gly Ala Thr Asp Phe Val Asn Pro Asn 225 230 235 240

- 56 -

Asp His Ala Lys Pro Ile Gln Asp Val Ile Val Glu Met Thr Asp Gly \$245\$

Gly Val Asp Tyr Ser Phe Glu Cys Ile Gly Ash Val Arg Leu Met Arg $260 \\ 265 \\ 270$

Ala Ala Leu Glu Cys Cys His Lys Gly Trp Gly Glu Ser Val Ile Ile 275 280 285

Gly Val Ala Pro Ala Gly Ala Glu Ile Asn Thr Arg Pro Phe His Leu 290 295 300

Val Thr Gly Arg Val Trp Arg Gly Ser Ala Phe Gly Gly Val Lys Gly 305 \$310\$ \$315

Arg Thr Glu Leu Pro Ser Tyr Val Glu Lys Ala Gln Gln Gly Glu Ile 325 330 335

Pro Leu Asp Thr Phe Ile Thr His Thr Met Gly Leu Asp Asp Ile Asn 340 345 350

Gln Leu Ser Arg

370

(2) INFORMATION FOR SEQ ID NO: 9:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1638 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..1635
 - (D) OTHER INFORMATION:/product=
 "gamma-Glutamylcystein-Synthetase"
 /gene= "gcs"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

ATG CCG CAA ACT CTT GCT GGA CGG TTG AGT CTG TTA TCC GGC ACC GAC Met Pro Gln Thr Leu Ala Gly Arg Leu Ser Leu Leu Ser Gly Thr Asp 375 380 385

	ACC Thr								96
	GTC Val								144
	GGC Gly								192
	CTG Leu								240
	GCT Ala 455								288
	GAG Glu								336
	CAA Gln								384
	CAC His								432
	TGC Cys								480
	GCT Ala 535								528
	CAG Gln								576
	TGG Trp								624
	TTC Phe								672

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							GAC Asp		720
							AAT Asn		768
							CCC Pro		816
							CGG Arg		864
							CTG Leu 675		912
							GCT Ala		960
							CTC Leu		1008
							CTC Leu		1056
							GAT Asp		1104
							CAA Gln 755		1152
							ATT Ile		1200
							TGT Cys		1248
							GCT Ala	TGG Trp	1296
							TCA Ser		1344

CAG Gln	GTG Val	CTC Leu	GCA Ala	GAG Glu 825	ATA Ile	CAC His	AGA Arg	CAC His	GGT Gly 830	GGG Gly	AGC Ser	TTC Phe	ACG Thr	GCA Ala 835	TTT Phe	1392
GGT Gly	CGC Arg	CAA Gln	TTA Leu 840	GCT Ala	ATC Ile	GAC Asp	CAT	GCA Ala 845	AAA Lys	CAC His	TTC Phe	AGT Ser	GCC Ala 850	TCC Ser	TCG Ser	1440
CTT Leu	GAG Glu	GCT Ala 855	GGC Gly	GTA Val	GCC Ala	AAA Lys	GCG Ala 860	CTT Leu	GAC Asp	CTC Leu	CAG Gln	GCG Ala 865	ACG Thr	TCG Ser	TCT Ser	1488
CTG Leu	CGC Arg 870	GAG Glu	CAG Gln	CAT His	CAA Gln	TTG Leu 875	GAG Glu	GCC Ala	AAC Asn	GAC Asp	CGT Arg 880	GCG Ala	CCA Pro	TTT Phe	TCT Ser	1536
GAC Asp 885	TAC Tyr	CTT Leu	CAG Gln	CAA Gln	TTC Phe 890	TCC Ser	CTG Leu	GCT Ala	TTC Phe	GGT Gly 895	CAA Gln	TCC Ser	GTC Val	GGC Gly	GCC Ala 900	1584
TCT Ser	CGT Arg	GCG Ala	CCC Pro	AAC Asn 905	CCT Pro	ACC Thr	GCG Ala	CAC His	CTC Leu 910	ATC Ile	GAT Asp	CTG Leu	ACC Thr	CCT Pro 915	CCT Pro	1632
GTC Val	TAA															1638

(2) INFORMATION FOR SEQ ID NO: 10:

- (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 545 amino acids
 - (A) BENGIN. 343 AMINO ACI
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:
- Met Pro Gln Thr Leu Ala Gly Arg Leu Ser Leu Leu Ser Gly Thr Asp $1 \hspace{1.5cm} 1 \hspace{1.5cm} 5 \hspace{1.5cm} 10$
- Glu Leu Thr Leu Leu Leu Arg Gly Gly Arg Gly Ile Glu Arg Glu Ala \$20\$
- Leu Arg Val Asp Val Gln Gly Glu Leu Ala Leu Thr Pro His Pro Ala 35 40 45
- Glu Ala Leu Leu Glu Leu Ile Thr Arg Pro Ala Thr Asp Cys Ala Gln 65 70 75 80

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Ala	Leu	Ala	Glu	Leu 85	Glu	Glu	Leu	His	Arg 90	Phe	Val	His	Ser	Arg 95	Leu
Glu	Gly	Glu	Tyr 100	Leu	Trp	Asn	Leu	Ser 105	Met	Pro	Gly	Arg	Leu 110	Pro	Val
Asp	Glu	Gln 115	Ile	Pro	Ile	Ala	Trp 120	Tyr	Gly	Pro	Ser	Asn 125	Pro	Gly	Met
Leu	Arg 130	His	Val	Tyr	Arg	Arg 135	Gly	Leu	Ala	Leu	Arg 140	Tyr	Gly	Lys	Arg
Met 145	Gln	Cys	Ile	Ala	Gly 150	Ile	His	Tyr	Asn	Tyr 155	Ser	Leu	Pro	Pro	Glu 160
Leu	Phe	Ala	Val	Leu 165	Thr	Lys	Ala	Glu	Val 170	Gly	Ser	Pro	Lys	Leu 175	Leu
Glu	Arg	Gln	Ser 180	Ala	Ala	Tyr	Met	Arg 185	Gln	Ile	Arg	Asn	Leu 190	Arg	Gln
Tyr	Gly	Trp 195	Leu	Leu	Ala	Tyr	Leu 200	Phe	Gly	Ala	Ser	Pro 205	Ala	Ile	Cys
Lys	Ser 210	Phe	Leu	Gly	Gly	Glu 215	Arg	Asp	Glu	Leu	Ala 220	Arg	Met	Gly	Gly
Asp 225	Thr	Leu	Tyr	Met	Pro 230	Tyr	Ala	Thr	Ser	Leu 235	Arg	Met	Ser	Asp	11e 240
Gly	Tyr	Arg	Asn	Arg 245	Ala	Met	Asp	Asp	Leu 250	Ser	Pro	Ser	Leu	Asn 255	Asp
Leu	Gly	Ala	Tyr 260	Ile	Arg	Asp	Ile	Cys 265	Arg	Ala	Leu	His	Thr 270	Pro	Asp
Ala	Gln	Tyr 275	Gln	Ala	Leu	Gly	Val 280	Phe	Ala	Gln	Gly	Glu 285	Trp	Arg	Gln
Leu	Asn 290	Ala	Asn	Leu	Leu	Gln 295	Leu	Asp	Ser	Glu	Tyr 300	Tyr	Ala	Leu	Ala
Arg 305	Pro	Lys	Ser	Ala	Pro 310	Glu	Arg	Gly	Glu	Arg 315	Asn	Leu	Asp	Ala	Leu 320
Ala	Arg	Arg	Gly	Val 325	Gln	Tyr	Val	Glu	Leu 330	Arg	Ala	Leu	Asp	Leu 335	Asp
Pro	Phe	Ser	Pro 340	Leu	Gly	Ile	Gly	Leu 345	Thr	Cys	Ala	Lys	Phe 350	Leu	Asp
Gly	Phe	Leu 355	Leu	Phe	Cys	Leu	Leu 360	Ser	Glu	Ala	Pro	Val 365	Asp	Asp	Arg

Asn Ala Gln Arg Ser Arg Pro Gly Lys Ser Glu Pro Gly Arg Gln Val

Arg Ala Ser Pro Gly Leu Lys Leu His Arg Asn Gly Gln Ser Ile Leu 385 390 395 400

Leu Lys Asp Trp Ala Gln Glu Val Leu Thr Glu Val Gln Ala Cys Val 405 410 415

Glu Leu Leu Asp Ser Ala Asn Gly Gly Ser Ser His Ala Leu Ala Trp \$420\$ \$425\$ \$430

Ser Ala Glu Glu Lys Val Leu Asn Pro Asp Cys Ala Pro Ser Ala 435 \$440\$

Gln Val Leu Ala Glu Ile His Arg His Gly Gly Ser Phe Thr Ala Phe 450 455 460

Gly Arg Gln Leu Ala Ile Asp His Ala Lys His Phe Ser Ala Ser Ser 465 470470475

Leu Glu Ala Gly Val Ala Lys Ala Leu Asp Leu Gln Ala Thr Ser Ser $485 \hspace{0.5cm} 495 \hspace{0.5cm}$

Leu Arg Glu Gln His Gln Leu Glu Ala Asn Asp Arg Ala Pro Phe Ser 500 505 510

Asp Tyr Leu Gln Gln Phe Ser Leu Ala Phe Gly Gln Ser Val Gly Ala 515 520 525

Ser Arg Ala Pro Asn Pro Thr Ala His Leu Ile Asp Leu Thr Pro Pro

Val 545

- (2) INFORMATION FOR SEQ ID NO: 11:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 354 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION:1..351

(D) OTHER INFORMATION:/product= "Cytochrom C UE-Eugenol-Hydroxylase" /gene= "ehyA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

		GTT Val							48
		CAG Gln 565	 	 	 		 	 	96
		ATT Ile						 	144
		GGC Gly						 	192
		ATC Ile							240
		ATG Met							288
		CTG Leu 645							336
		GCG Ala	TGA						354

(2) INFORMATION FOR SEO ID NO: 12:

660

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 117 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

Met Met Asn Val Asn Tyr Lys Ala Val Gly Ala Ser Leu Leu Leu Ala 1 5

Phe Ile Ser Gln Gly Ala Trp Ala Glu Ser Pro Ala Ala Ser Gly Asn 20 25 30

COVECUES THEROO

150

Thr Pro Asp Ile Tyr Arg Lys Thr Cys Thr Tyr Cys His Glu Pro Thr Val Asn Asn Gly Arg Val Ile Ala Arg Ser Leu Gly Pro Thr Leu Arg 55 Gly Arg Gln Ile Pro Pro Gln Tyr Thr Glu Tyr Met Val Arg His Gly Arg Gly Ala Met Pro Ala Phe Ser Glu Ala Glu Val Pro Pro Ala Glu Leu Lys Val Leu Gly Asp Trp Ile Gln Gln Ser Ser Ala Pro Lys Asp 100 105 Ala Gly Val Ala Pro 115 (2) INFORMATION FOR SEQ ID NO: 13: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 687 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear (ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION:1..684 (D) OTHER INFORMATION:/gene= "ORF5" (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13: ATG ACT ACC CGT CGC AAC TTT CTA ATA GGC GCG TCG CAG GTG GGG GCA Met Thr Thr Arg Arg Asn Phe Leu Ile Gly Ala Ser Gln Val Gly Ala 120 TTG GTG ATG ATG TCG CCG AAA TTG GTC TTC CGT ACG CCG CTC AAG CAG 96 Leu Val Met Met Ser Pro Lys Leu Val Phe Arg Thr Pro Leu Lys Gln 135 140 AAG CCC GTG CGC ATC CTG TCG ACC GGG CTG GCC GGT GAG CAA GAG TTT 144

Lys Pro Val Arg Ile Leu Ser Thr Gly Leu Ala Gly Glu Gln Glu Phe

													CAG				192
	His	Ser	Met	Leu	_	Ala	Arg	Leu	Thr		Thr	Gly	Gln	Val	-	Ile	
					170					175					180		
	ccc	TCG	CTD)	CCG	CTC	GNC	CCN	CCT	ייייית	TGG	com	m/cm	ccc	CCT	CCA	CTT	240
													Pro				240
				185	200	. iop			190					195		200	
	GCC	CAG	GCA	ATG	GAT	GCG	TTG	AAT	GGT	ACG	CGT	CTG	ATC	GCT	TTT	GTT	288
	Ala	Gln	Ala	Met	Asp	Ala	Leu	Asn	Gly	Thr	Arg	Leu	Ile	Ala	Phe	Val	
			200					205					210				
													ATG				336
	Glu		Arg	Asn	Glu	Leu		Leu	Met	Gln	Phe		Met	Asp	Arg	Gly	
		215					220					225					
	COT	ccc	CTC	cmm	z, mm	CD D	ccm	CAC	C T III	ccc	cmc	CDC	AGC	77.7	ccc	CMC	384
													Ser				304
	230	MIG	val	лец	rre	235	GLY	GIU	nis	MIA	240	Мэр	Ser	шуз	GLY	245	
had	200					200					210					245	
ų.	TCT	CGG	CAC	GAC	TTT	CTG	AGT	ACC	CCA	TCC	AGT	GCG	GGA	ATT	GGA	GGG	432
76	Ser	Arg	His	Asp	Phe	Leu	Ser	Thr	Pro	ser	Ser	Ala	Gly	Ile	Gly	Gly	
15					250					255					260		
O																	
47	GCG	CTA	GCC	GAC	AGC	CTG	GCA	AAA	GGG	GGC	TCG	CCG	TTC	TCT	ATT	TCC	480
00	Ala	Leu	Ala		Ser	Leu	Ala	Lys	-	Gly	Ser	Pro	Phe		Ile	Ser	
(F)				265					270					275			
8	cmc	007	cac	cmm.	000	mac	cm n	3 cm	com	an c	003	T C T	T. COM	7 7 M	an.a	n.cm	500
poli es s													AGT Ser				528
N	Val	Arg	280	пец	GTA	ser	val	285	ALA	GIII	PLO	ALG	290	ASII	GIII	ser	
n m			200					200									
0	GAG	GTG	GCC	ACC	CAC	TGG	ACG	ACC	GCT	CTG	GGG	ACC	TAT	TAT	GCC	GAT	576
344													Tyr				
lead.		295					300					305				-	
	ATC	GCA	GTG	GGG	CGC	TGG	GAG	CCG	CAG	CGC	GAA	GTG	GCC	AGC	TAT	GGA	624
		Ala	Val	Gly	Arg		Glu	Pro	Gln	Arg		Val	Ala	Ser	Tyr		
	310					315					320					325	
	AGT	GGA	CTD	NTC.	лтс	ccc	CDD	cee	CTPTP	CAT	CCT	CTT	GCC	TCD	ncc.	mm.c	672
													Ala				0/2
		J y			330	- 12.4	J_ 4	- 12-9	Lea	335	9	,		J-1	340		
	ATT	GCA	GAT	CTC	TGA												687
	Ile	Ala	Asp	Leu													
				345													

(2) INFORMATION FOR SEQ ID NO: 14:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 228 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

Met Thr Thr Arg Arg Asn Phe Leu Ile Gly Ala Ser Gln Val Gly Ala

Leu Val Met Met Ser Pro Lys Leu Val Phe Arg Thr Pro Leu Lys Gln

Lys Pro Val Arg Ile Leu Ser Thr Gly Leu Ala Gly Glu Gln Glu Phe 40

His Ser Met Leu Arg Ala Arg Leu Thr His Thr Gly Gln Val Asp Ile 55

Ala Ser Val Pro Leu Asp Ala Ala Ile Trp Ala Ser Pro Ala Arg Leu

Ala Gln Ala Met Asp Ala Leu Asn Gly Thr Arg Leu Ile Ala Phe Val 90

Glu Pro Arg Asn Glu Leu Ile Leu Met Gln Phe Leu Met Asp Arg Gly 100

Ala Ala Val Leu Ile Gln Gly Glu His Ala Val Asp Ser Lys Gly Val 115 120

Ser Arg His Asp Phe Leu Ser Thr Pro Ser Ser Ala Gly Ile Gly Gly 130 135

145 150 Val Arg Ala Leu Gly Ser Val Thr Ala Gln Pro Arg Ser Asn Gln Ser

Glu Val Ala Thr His Trp Thr Thr Ala Leu Gly Thr Tyr Tyr Ala Asp 180

Ile Ala Val Gly Arg Trp Glu Pro Gln Arg Glu Val Ala Ser Tyr Gly 200

Ser Gly Leu Ile Met Ala Glu Arg Leu Asp Arg Val Ala Ser Thr Phe

Ile Ala Asp Leu 225

- (2) INFORMATION FOR SEQ ID NO: 15:
 - (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1554 base pairs
 - (B) TYPE: nucleic acid

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N Ala Leu Ala Asp Ser Leu Ala Lys Gly Gly Ser Pro Phe Ser Ile Ser

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				STRAI TOPO:				ıble								
	(i:	i) M	OLEC	JLE :	TYPE:	: DNA	A (ge	enomi	ic)							
	(ii:	i) H	YPOTI	HETI	CAL:	NO										
	(i	v) Al	TI-:	SENSI	s: No)										
	(i:		EATUI	RE: VAME/	KEY:	CDS	:									
			(B) I	LOCAT	:NOI	11	551	I - /n s	odue	1	. m.)	opro				
				UE	:-Eug	genol	-нус	lroxy	lase	"	riav	opro	teln			
				7 9	ene=	er.	iya									
	(xi) SE	QUEN	ICE I	ESCR	IPTI	on:	SEQ	ID N	io: 1	5:					
ATO	GA/	A AGO	ACC	GT#	GTT	CTT	ccc	GAG	GGT	GTC	ACC	CCG	GAG	CAG	TTC	48
Met	: Gli 230	Ser	Thr	: Val	Val	235		Glu	Gly	Val	Thr 240		Glu	Gln	Phe	
ACC	AAF	GCC	ATC	AGC	GAG	TTC	CGT	CAG	GTA	TTG	GGT	GAG	GAC	AGT	GTT	96
Thr 245	Lys	Ala	Ile	Ser	G1u 250	Phe	Arg	Gln	Val	Leu 255	Gly	Glu	Asp	Ser	Val	30
CTT	GTC	ACT	GCT	AAD			GTT.	ccc	יימיי			CTC	cmc	7. mm		
Leu	Val	Thr	Ala	Glu 265	Arg	Val	Val	Pro	Tyr 270	Thr	Lys	Leu	Leu	Ile	Pro	144
DCD	CAG	C D TT	CDm			ma c	T.00							275		
Thr	Gln	Asp	Asp	Ala	Gln	Tyr	Thr	Pro	Ala	Gly	Ala	TTG Leu	ACT Thr	Pro	TCT	192
			280					285					290			
TCG Ser	GTG Val	GAG Glu	CAG Gln	GTC Val	CAG Gln	AAA Lys	GTC Val	ATG Met	GGG Gly	ATC Ile	TGC	AAT Asn	AAG Lvs	TAC	AAG	240
		295					300		_		-	305	-2-	-,-	-,-	
ATC Ile	CCG	GTA Val	TGG	CCA	ATC	TCT	ACC	GGT	CGG	AAC	TGG	GGG Gly	TAT	GGG	TCC	288
	310				110	315		OLY	ALG	Aon	320	сту	TYE	сту	ser	
GCT	TCG	CCT	GCA	ACT	CCT	GGG	CAG	ATG	ATT	CTT	GAC	CTT	CGC	AAG	ATG	336
325	Ser	FIO	ALG	THE	330	сту	GIN	Met	IIe	1.eu 335	Asp	Leu	Arg	Lys	Met 340	
AAC	AAG	ATC	ATT	GAG	ATC	GAT	GTT	GAG	GGG	TGT	ACT	GCC	CTG	CTC	GAG	384
Asn	Lys	Ile	Ile	Glu 345	Ile	Asp	Val	Glu	Gly 350	Cys	Thr	Ala	Leu	Leu 355	Glu	
CCG	GGC	GTT	ACC	TAC	CAG	CAG	CTT	CAC	GAT	TAC	ATC	AAG	GAG	CAC	AAT	432
Pro	Gly	Val	Thr	Tyr	Gln	Gln	Leu	His	Asp	Tyr	Ile	Lys	Glu	His	Asn	.52

365

CTC	CCC Pro	Leu 375	Met	CTG Leu	GAT Asp	GTG Val	Pro 380	Thr	ATT	GGG Gly	CCT Pro	Met 385	Val	GGC Gly	CCG Pro	480
GT6	GGT Gly 390	Asn	ACG Thr	CTG Leu	GAT Asp	CGA Arg 395	Gly	GTT Val	GGT Gly	TAT	ACG Thr 400	Pro	TAC	GGC Gly	GAG Glu	528
CAC His 405	TTC Phe	ATG Met	ATG Met	CAG Gln	TGT Cys 410	Gly	ATG Met	GA.A Glu	GTC Val	GTC Val 415	ATG Met	GCC	GAT Asp	GGC Gly	GAA Glu 420	576
ATC Ile	CTC Leu	CGT Arg	ACT Thr	GGT Gly 425	ATG Met	GGC Gly	TCG Ser	GTG Val	Pro 430	Lys	GCC Ala	AAG Lys	ACT Thr	TGG Trp 435	CAG Gln	624
GCA Ala	TTC Phe	AAA Lys	TGG Trp 440	GGC Gly	TAT Tyr	GGT Gly	CCA Pro	TAT Tyr 445	CTG Leu	GAC Asp	GGT Gly	ATC Ile	TTT Phe 450	ACC Thr	CAG Gln	672
TCC	AAC Asn	TTT Phe 455	GGT Gly	GTT Val	GTG Val	ACA Thr	AAG Lys 460	CTC Leu	GGG Gly	ATT Ile	TGG Trp	TTG Leu 465	ATG Met	CCC Pro	AAG Lys	720
CCG Pro	CCA Pro 470	GTG Val	ATC Ile	AAG Lys	TCG Ser	TTT Phe 475	ATG Met	ATC Ile	CGT Arg	TAT Tyr	CCC Pro 480	AAT Asn	GAA Glu	GCT Ala	GAT Asp	768
GTG Val 485	GTT Val	AAG Lys	GCA Ala	ATT Ile	GAT Asp 490	GCT Ala	TTT Phe	CGC Arg	CCG Pro	CTG Leu 495	CGT Arg	ATT Ile	ACT Thr	CAG Gln	CTG Leu 500	816
ATT Ile	CCT Pro	AAC Asn	GTC Val	GTT Val 505	TTG Leu	TTC Phe	ATG Met	CAC His	GGC Gly 510	ATG Met	TAC Tyr	GAA Glu	ACG Thr	GCA Ala 515	ATC Ile	864
TGC Cys	CGG Arg	ACG Thr	CGT Arg 520	GCT Ala	GAG Glu	GTT Val	ACT Thr	TCG Ser 525	GAC Asp	CCA Pro	GGT Gly	CCT Pro	ATT Ile 530	TCT Ser	GAA Glu	912
GCG Ala	GAC Asp	GCC Ala 535	CGC Arg	AAA Lys	GCA Ala	TTC Phe	AAA Lys 540	GAG Glu	CTA Leu	GGC Gly	GTT Val	GGC Gly 545	TAC Tyr	TGG Trp	AAC Asn	960
GTT Val	TAC Tyr 550	TTC Phe	GCG Ala	CTT Leu	TAC Tyr	GGC Gly 555	ACA Thr	GAA Glu	GAG Glu	Gln	ATA Ile 560	GCC Ala	GTC Val	AAT Asn	GAA Glu	1008
AAG Lys 565	ATC Ile	GTC Val	CGC Arg	Gly	ATC Ile 570	CTC Leu	GAA Glu	CCG Pro	Thr	GGG Gly 575	GGT Gly	GAG Glu	ATC Ile	CTC Leu	ACC Thr 580	1056

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GAA Glu	GAG Glu	GAG Glu	GCT Ala	Gly	GAT Asp	AAC Asn	ATT Ile	CTT Leu	Phe	His	CAC	CAT His	AAG Lys	CAG Gln	CTC Leu	1104
ATG	AAC	GGC	GAG	585 ATG	aca	TTG	GAG	CDD	590		n.m.c	mn.c	CDC	595	222	
Met	Asn	Gly	Glu 600	Met	Thr	Leu	Glu	G1u 605	Met	Asn	Ile	Tyr	Gln 610	Trp	Arg	1152
GGA	GCA	GGT	GGC	GGT	GCT	TGC	TGG	TTT	GCA	CCG	GTT	GCT	CAG	GTC	AAG	1200
GIY	ALA	615	GIĀ	GIY	Ala	Cys	620	Phe	Ala	Pro	Val	Ala 625	Gln	Val	Lys	
GGG Glv	CAT	GAG G1 u	GCA	GAG	CAG Gln	CAG	GTC	AAG	CTT	GCT	CAG	AAG	GTG	CTT	GCA	1248
	630					635					640					
AAG	CAT	GGG G1 v	TTC	GAT	TAC Tyr	ACG	GCG	GGC	TTT	GCG	ATT	GGT	TGG	CGC	GAT	1296
645					650					655			_		660	
CTT	CAC	CAT	GTG Val	ATC	GAT Asp	GTG	CTG	TAC	GAC	CGT	AGC	AAT	GCC	GAC	GAG	1344
				665					670					675		
AAA	AAG	CGC	GCT	TAC	GCT Ala	TGC	TTT	GAT	GAA	TTG	ATC	GAC	GTC	TTT	GCG	1392
			680					685					690			
GCC	GAA	GGC G1 v	TTT	GCA	AGT Ser	TAC	AGG	ACC	AAT	ATT	GCC	TTT	ATG	GAC	AAA	1440
		695					700					705			-	
GTC	GCC	TCT	AAG	TTC	GGC	GCT	GAG	AAT	AAG	AGG	GTC	AAT	CAG	AAG	ATC	1488
	710				Gly	715					720			-		
AAG	GCT	GCC	CTT	GAT	CCA	AAC	GGC	ATC	ATC	GCT	CCC	GGC	AAG	TCG	GGC	1536
725					Pro 730	ASII	стА	тте	тте	735	rro	GTÀ	ьys	ser	Gly 740	
ATT		CTT Leu			TAA											1554

(2) INFORMATION FOR SEQ ID NO: 16:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 517 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

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Met Glu Ser Thr Val Val Leu Pro Glu Gly Val Thr Pro Glu Gln Phe Thr Lys Ala Ile Ser Glu Phe Arg Gln Val Leu Gly Glu Asp Ser Val Leu Val Thr Ala Glu Arg Val Val Pro Tvr Thr Lvs Leu Leu Ile Pro Thr Gln Asp Asp Ala Gln Tyr Thr Pro Ala Gly Ala Leu Thr Pro Ser Ser Val Glu Gln Val Gln Lys Val Met Gly Ile Cys Asn Lys Tyr Lys Ile Pro Val Trp Pro Ile Ser Thr Gly Arg Asn Trp Gly Tyr Gly Ser Ala Ser Pro Ala Thr Pro Gly Gln Met Ile Leu Asp Leu Arg Lys Met 105 100 Asn Lys Ile Ile Glu Ile Asp Val Glu Gly Cys Thr Ala Leu Leu Glu 120 Pro Gly Val Thr Tyr Gln Gln Leu His Asp Tyr Ile Lys Glu His Asn Leu Pro Leu Met Leu Asp Val Pro Thr Ile Gly Pro Met Val Gly Pro 150 [Val Gly Asn Thr Leu Asp Arg Gly Val Gly Tyr Thr Pro Tyr Gly Glu His Phe Met Met Gln Cys Gly Met Glu Val Val Met Ala Asp Gly Glu Ile Leu Arg Thr Gly Met Gly Ser Val Pro Lys Ala Lys Thr Trp Gln 200 Ala Phe Lys Trp Gly Tyr Gly Pro Tyr Leu Asp Gly Ile Phe Thr Gln Ser Asn Phe Gly Val Val Thr Lys Leu Gly Ile Trp Leu Met Pro Lys Pro Pro Val Ile Lys Ser Phe Met Ile Arg Tyr Pro Asn Glu Ala Asp 245 250 Val Val Lys Ala Ile Asp Ala Phe Arg Pro Leu Arg Ile Thr Gln Leu

Ile Pro Asn Val Val Leu Phe Met His Gly Met Tyr Glu Thr Ala Ile 280

Ala Asp Ala Arg Lys Ala Phe Lys Glu Leu Gly Val Gly Tyr Trp Asn 310

Val Tyr Phe Ala Leu Tyr Gly Thr Glu Glu Gln Ile Ala Val Asn Glu 330

Lys Ile Val Arg Gly Ile Leu Glu Pro Thr Gly Gly Glu Ile Leu Thr 340

Glu Glu Glu Ala Gly Asp Asn Ile Leu Phe His His His Lys Gln Leu

Met Asn Gly Glu Met Thr Leu Glu Glu Met Asn Ile Tyr Gln Trp Arq 375

Gly Ala Gly Gly Gly Ala Cys Trp Phe Ala Pro Val Ala Gln Val Lys 385

Gly His Glu Ala Glu Gln Gln Val Lys Leu Ala Gln Lys Val Leu Ala

Lys His Gly Phe Asp Tyr Thr Ala Gly Phe Ala Ile Gly Trp Arg Asp 420

Leu His His Val Ile Asp Val Leu Tyr Asp Arg Ser Asn Ala Asp Glu

Lys Lys Arg Ala Tyr Ala Cys Phe Asp Glu Leu Ile Asp Val Phe Ala 455

Ala Glu Gly Phe Ala Ser Tyr Arg Thr Asn Ile Ala Phe Met Asp Lys 465 470

Val Ala Ser Lys Phe Gly Ala Glu Asn Lys Arg Val Asn Gln Lys Ile 490

Lys Ala Ala Leu Asp Pro Asn Gly Ile Ile Ala Pro Gly Lys Ser Gly 505 510

Ile His Leu Pro Lys 515

- (2) INFORMATION FOR SEQ ID NO: 17:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 861 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

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(iii)	HYPOTHETICAL:	NO

(iv) ANTI-SENSE: NO

(ix) FEATURE:

665

- (A) NAME/KEY: CDS
- (B) LOCATION:1..858
- (D) OTHER INFORMATION:/gene= "ORF2"

(X1) SEQUENCE DESCRIPTION: SEQ ID NO: 17: ATG ATT GCA ATC ACT GCG GGC ACC GGA AGT CTT GGT CGG GCT ATC GTT 46																	
ATG Met	ATT Ile	GCA Ala 520	Ile	ACT Thr	GCG Ala	GGC Gly	Thr 525	Gly	AGT Ser	CTT Leu	GGT Gly	CGG Arg 530	Ala	ATC	GTT Val		48
GAG Glu	CGA Arg 535	Leu	. GGG : Gly	GAC Asp	TGC Cys	GGT Gly 540	Leu	ATC	GGT	CAA Gln	GTT Val 545	Arg	TTG Leu	ACG Thr	GCT Ala		96
CGC Arg 550	Asp	CCT	AAA Lys	AGG Arg	CTT Leu 555	CGT Arg	GCC Ala	GCT Ala	GCC Ala	GAG Glu 560	GAA Glu	GGG Gly	TTT	CAG Gln	GTC Val 565		144
GCT Ala	AAG Lys	GCG Ala	GAT Asp	TAC Tyr 570	GCC Ala	GAT Asp	ATT	GGG Gly	AGT Ser 575	CTT Leu	GAC Asp	CAG Gln	GCA Ala	TTA Leu 580	CAG Gln		192
GGG Gly	GTA Val	GAC Asp	GTA Val 585	TTA Leu	CTC Leu	CTG Leu	ATT Ile	TCT Ser 590	GGT Gly	ACT Thr	GCA Ala	CCC Pro	AAT Asn 595	GAA Glu	ATA Ile		240
AGG Arg	ATC Ile	CAA Gln 600	CAG Gln	CAT His	AAG Lys	TCG Ser	GTC Val 605	ATC Ile	GAC Asp	GCG Ala	GCA Ala	AAA Lys 610	CGA Arg	AAC Asn	GGC Gly		288
GTG Val	TCG Ser 615	CGT Arg	ATT Ile	GTG Val	TAT Tyr	ACC Thr 620	AGC Ser	TTC Phe	ATA Ile	AAT Asn	CCA Pro 625	AGT Ser	ACT Thr	CGC Arg	AGC Ser		336
AGG Arg 630	TCT Ser	ATT Ile	TGG Trp	GCC Ala	TCC Ser 635	ATT Ile	CAT His	CGT Arg	GAA Glu	ACT Thr 640	GAG Glu	ACT Thr	TAC Tyr	CTC Leu	AGG Arg 645		384
CAG Gln	TCT Ser	GGG Gly	GTG Val	AAG Lys 650	TTT Phe	ACG Thr	ATT Ile	GTC Val	CGA Arg 655	AAT Asn	AAT Asn	CAG Gln	TAT Tyr	GCG Ala 660	TCT Ser		432
AAC Asn	CTG Leu	GAT Asp	CTG Leu 665	TTG Leu	CTG Leu	Leu	Arg	Ala	CAA Gln	Asp	Ser	GGA Gly	ATA Ile	TTT Phe	GCC Ala		480

670

								GAC Asp	528
								AAC Asn	 576
								ATC Ile	624
								GAT Asp 740	672
								CCT Pro	 720
								GCT Ala	768
								CGA Arg	816
	GAA Glu								858
TGA									861

- (2) INFORMATION FOR SEQ ID NO: 18:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 286 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

Met Ile Ala Ile Thr Ala Gly Thr Gly Ser Leu Gly Arg Ala Ile Val $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Glu Arg Leu Gly Asp Cys Gly Leu Ile Gly Gln Val Arg Leu Thr Ala 20 25 30

Arg Asp Pro Lys Arg Leu Arg Ala Ala Ala Glu Glu Gly Phe Gln Val\$35\$

- Ala Lys Ala Asp Tyr Ala Asp Ile Gly Ser Leu Asp Gln Ala Leu Gln 50 55 60
- Gly Val Asp Val Leu Leu Leu Ile Ser Gly Thr Ala Pro Asn Glu Ile 65 7075 75
- Arg Ile Gln Gln His Lys Ser Val Ile Asp Ala Ala Lys Arg Asn Gly \$85\$
- Val Ser Arg Ile Val Tyr Thr Ser Phe Ile Asn Pro Ser Thr Arg Ser $100 \\ 105 \\ 110$
- Arg Ser Ile Trp Ala Ser Ile His Arg Glu Thr Glu Thr Tyr Leu Arg 115 120 125
- Gln Ser Gly Val Lys Phe Thr Ile Val Arg Asn Asn Gln Tyr Ala Ser 130 135 140
- Asn Leu Asp Leu Leu Leu Leu Arg Ala Gln Asp Ser Gly Ile Phe Ala 145 \$150\$
- Ile Pro Gly Ala Lys Gly Arg Val Ala Tyr Val Ser His Arg Asp Val
- Ala Ala Ala Ile Cys Ser Val Leu Thr Thr Ala Gly His Asp Asn Arg 180 \$180\$
- Ile Tyr Gln Leu Thr Gly Ser Glu Ala Leu Asn Gly Leu Glu Ile Ala 195 200 205
- Glu Ile Leu Gly Gly Val Leu Gly Arg Pro Val Arg Ala Met Asp Ala 210 215 220
- Ser Pro Asp Glu Phe Ala Ala Ser Phe Arg Glu Ala Gly Phe Pro Glu 225 230 235 240
- Phe Met Val Glu Gly Leu Leu Ser Ile Tyr Ala Ala Ser Gly Ala Gly 245 250 255
- Glu Tyr Gln Ser Val Ser Pro Asp Val Gly Leu Leu Thr Gly Arg Arg $260 \hspace{1.5cm} 265 \hspace{1.5cm} 270 \hspace{1.5cm}$
- Ala Glu Ser Met Arg Thr Tyr Ile Gln Arg Leu Val Trp Pro 275 280 285
- (2) INFORMATION FOR SEQ ID NO: 19:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1011 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(ix) FEATURE:

(A) NAME/KEY: CDS

435

- (B) LOCATION:1..1008
- (D) OTHER INFORMATION:/product= "Alkohol-Dehydrogenase" /gene= "adh"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

	AAG Lys									48
	CAG Gln									96
	AGG Arg 320									144
	GGT Gly									192
	GGT G1 y									240
	CAG Gln									288
	AAG Lys									336
	GGG Gly 400							ATA Ile	-	384
	ATA Ile									432
	GCG Ala									480

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1011

GCC GGT GAT ACG GTC TTG TTG CTT GGC ACT GGC GGT GTC TCG ATG TTC

(2) INFORMATION FOR SEQ ID NO: 20:

BOLS.

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 336 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

Met Lys Ala Tyr Glu Leu His Lys Ile Ser Glu Gln Val Glu Val Arg 1 5 10 15

Leu Gln Pro Thr Arg Pro Arg Pro Gln Leu Asn His Gly Glu Val Leu 20 25 30

Ile Arg Val His Ala Ala Ser Leu Asn Phe Arg Asp Leu Met Ile Leu $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$

Ala Gly Arg Tyr Pro Gly Gln Met Lys Pro Asp Val Ile Pro Leu Ser 50 60

Asp Gly Ala Gly Glu Ile Val Glu Val Gly Pro Gly Val Ser Ser Glu 65 70 75 80

Gly Lys Ile Thr Glu Pro Ala Ile Glu Val Ser Leu Gly Phe Gly Met 100 \$105\$

Asp Gly Met Leu Ala Glu Tyr Val Ala Leu Pro Tyr Glu Ala Thr Ile 115 $$\rm 120$$

Pro Ile Pro Glu His Leu Ser Tyr Glu Glu Ala Ala Thr Leu Pro Cys 130 135 140

Ala Ala Leu Thr Ala Trp Asn Ala Leu Thr Glu Val Gly Arg Val Lys $145 \hspace{1.5cm} 150 \hspace{1.5cm} 155 \hspace{1.5cm} 160$

Ala Gly Asp Thr Val Leu Leu Gly Thr Gly Gly Val Ser Met Phe \$165\$ \$170\$ \$175\$

Ser Ser Glu Gln Lys Leu Glu Arg Val Lys Ala Met Gly Ala Asp His $195 \hspace{1.5cm} 200 \hspace{1.5cm} 205 \hspace{1.5cm}$

Leu Ile Asn Tyr Arg Asn Ser Pro Gly Trp Asp Arg Thr Val Leu Asp 210 \$215\$

Leu Thr Ala Gly Arg Gly Val Asp Leu Val Val Glu Val Gly Gly Ala 225 230 235 240

Gly Thr Leu Glu Arg Ser Leu Arg Ala Val Lys Val Gly Gly Ile Val 245 250 255

Ala Thr Ile Gly Leu Val Ala Gly Val Gly Pro Ile Asp Pro Leu Pro 260 265 270

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Leu Ile Ser Arg Ala Ile Gln Leu Ser Gly Val Tyr Val Gly Ser Arg 275 280 285	
Glu Met Phe Leu Ser Met Asn Lys Ala Ile Ala Ser Ala Glu Ile Lys 290 295 300	
Pro Val Ile Asp Cys Phe Pro Ile Asp Glu Val Gly Asp Ala Tyr 305 310 315	
Glu Tyr Met Arg Ser Gly Asn His Leu Gly Lys Val Val Ile Thr Ile 325 330 335	
(2) INFORMATION FOR SEQ ID NO: 21: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1518 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear (ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (ix) FEATURE: (A) NAMME/KEY: CDS (B) LOCATION: complement (41518) (D) OTHER INFORMATION:/product= "Lignostilben-Dioxygenase" //gene= "lsd"	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:	
TCACCGTCGT GATCGGGATT GGAAATTCGT GCGAGGACAG CGGCCACGTA CCGGCGCCCCT	60
GAAGGGCTGG AAGGTTGGAG TTTCGTTAAG GTCTGGTACC CAGCAGCCAT GGAGAGCGGC	120
CCTTAGCCGG AATGGCAGCT TGATGGTTGC CACGGGACCA GACTGGATGT CTTGAGTGTC	180
GAGAATTACC AGATCGCTGC GATTTTCATC GAGGCGACCA ACCACGGTCA GCAAGTACCC	240
GTCACCTTCG GCGGCGGTCG GACTTCTAGG GACGAAGGCC GGCTCCTGGG CCGCCGAGGC	300
TTCGCCGGAG TACCAGAGGT CGTAGTCACC TCGGTGGTTG TCCCAGATGC CGAGTGAGTT	360
GTACGCGAAT ATCTTCTCGG CCTGCTGATG CGCAAGTGGT TTGCGTGGAT CGTCCACCCC	420
CATAAAGCCA TAGCGGTTGC ATTGCAGGGC GAACGAAGAA TCCATGATTG GCATTTCCGC	480
AAAGAAATCG TGTAGCCGGG TTCGCTTGAT CTCGTCGCTG CTGCTATCGA GGTCAATTTC	540

AAAGAAATCG TGTAGCCGGG TTCGCTTGAT CTCGTCGCTG CTGCTATCGA GGTCAATTTC

600

660

1518

CCAACGAGTC AGGCGTGGTA CGGCTTTCTC AGGGGCGAAG GGTTGGTTTT GTGAGTTGGG

GAAGGGGAAC GGCAGGATTT CACTITCCAT AAGGTCGATA TAAATCTTGG TTCCGACTTC

(2) INFORMATION FOR SEQ ID NO: 22:

GCGGTTGAAT CTCGCCAT

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 505 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

Met Ala Arg Phe Asn Arg Asn Asp Pro Gln Leu Val Gly Thr Leu Leu 1 5 10 15

Pro Thr Arg Ile Glu Ala Asp Leu Phe Asp Leu Glu Val Asp Gly Glu $20 \ 25 \ 30$

Ile Pro Lys Ser Ile Asn Gly Thr Phe Tyr Arg Asn Thr Pro Glu Pro $35 \ \ 40 \ \ 45$

Gln Val Thr Pro Gln Lys Phe His Thr Phe Ile Asp Gly Asp Gly Met

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Ala Ser Ala Phe His Phe Glu Asp Gly His Val Asp Phe Ile Ser Arg $65 \hspace{1.5cm} 70 \hspace{1.5cm} 75 \hspace{1.5cm} 80$

Trp Val Lys Thr Ala Arg Phe Thr Ala Glu Arg Leu Ala Arg Lys Ser 85 90 95

Leu Phe Gly Met Tyr Arg Asn Pro Tyr Thr Asp Asp Thr Ser Val Lys \$100\$

Gly Leu Asp Arg Thr Val Ala Asn Thr Ser Ile Ile Ser His His Gly 115 120 125

Lys Val Leu Ala Val Lys Glu Asp Gly Leu Pro Tyr Glu Leu Asp Pro 130 135 140

Arg Thr Leu Glu Thr Arg Gly His Phe Asp Tyr Asp Gly Gln Val Thr 145 150 155 160

Ser Gln Thr His Thr Ala His Pro Lys Tyr Asp Pro Glu Thr Gly Asp \$165\$ \$170\$ \$175\$

Leu Leu Phe Phe Gly Ser Ala Ala Lys Gly Glu Ala Thr Pro Asp Met 180 185 190

Ala Tyr Tyr Ile Val Asp Lys His Gly Lys Val Thr His Glu Thr Trp

Phe Glu Gln Pro Tyr Gly Ala Phe Met His Asp Phe Ala Ile Thr Arg 210 215 220

Asn Trp Ser Ile Phe Pro Ile Met Pro Ala Thr Asn Ser Leu Ser Arg 225 230 235 240

Leu Lys Ala Lys Gln Pro Ile Tyr Met Trp Glu Pro Glu Leu Gly Ser 245 250 255

Tyr Ile Gly Val Leu Ala Pro Arg Gln Gly Ser Leu Ile Arg Trp Leu 260 265 270

Lys Ala Pro Ala Leu Trp Val Phe His Val Val Asn Ala Trp Glu Val 275 280 285

Gly Thr Lys Ile Tyr Ile Asp Leu Met Glu Ser Glu Ile Leu Pro Phe 290° $$ 300 $$

Pro Phe Pro Asn Ser Gln Asn Gln Pro Phe Ala Pro Glu Lys Ala Val 305 \$310\$ 315 320

Pro Arg Leu Thr Arg Trp Glu Ile Asp Leu Asp Ser Ser Ser Asp Glu 325 330 335 Ile Lys Arg Thr Arg Leu His Asp Phe Phe Ala Glu Met Pro Ile Met 340 345 350

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Asp Ser Ser Phe Ala Leu Gln Cys Asn Arg Tyr Gly Phe Met Gly Val \$355\$ \$360\$

Ala Tyr Asn Ser Leu Gly Ile Trp Asp Asn His Arg Gly Asp Tyr Asp 385 \$390\$

Leu Trp Tyr Ser Gly Glu Ala Ser Ala Ala Glu Glu Pro Ala Phe Val \$405\$

Pro Arg Ser Pro Thr Ala Ala Glu Gly Asp Gly Tyr Leu Leu Thr Val \$420\$

Val Gly Arg Leu Asp Glu Asn Arg Ser Asp Leu Val Ile Leu Asp Thr 435 440 445

Gln Asp Ile Gln Ser Gly Pro Val Ala Thr Ile Lys Leu Pro Phe Arg 450 455 460

Leu Arg Ala Ala Leu His Gly Cys Trp Val Pro Asp Leu Asn Glu Thr $465 \hspace{1.5cm} 470 \hspace{1.5cm} 475 \hspace{1.5cm} 480 \hspace{1.5cm}$

Pro Thr Phe Gln Pro Phe Arg Ala Pro Val Arg Gly Arg Cys Pro Arg 485 490495

Thr Asn Phe Gln Ser Arg Ser Arg Arg 500 505

- (2) INFORMATION FOR SEQ ID NO: 23:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 951 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..948
 - (D) OTHER INFORMATION:/gene= "ORF3"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID No: 23:

ATG Met	ACA Thr	ACT Thr	ATT Ile	CGG Arg 510	TGG Trp	CGG Arg	CGT Arg	ATG Met	TCC Ser 515	ATT Ile	CAC His	TCT Ser	GAG Glu	GGG Gly 520	ATC Ile	48
												CTG Leu				96
												GGT Gly 550				144
												TAC Tyr				192
												CGA Arg				240
												GGC Gly				288
GTT Val	GCA Ala	TCC Ser	GGC Gly 605	GGA Gly	AGA Arg	AAG Lys	GTG Val	ATC Ile 610	TTG Leu	GCA Ala	AAT Asn	GGT Gly	GAT Asp 615	TGC Cys	TCC Ser	336
ATA Ile	GTT Val	GAT Asp 620	AGT Ser	CGC Arg	CAA Gln	GAC Asp	TTC Phe 625	ACA Thr	CTT Leu	TCC	TCG Ser	AAC Asn 630	TCT Ser	TCG Ser	ACC Thr	384
												GGA Gly			GTG Val	432
TCC Ser 650	AAT Asn	CCG Pro	GAG Glu	GAT Asp	CTT Leu 655	ATC Ile	GCC Ala	CGA Arg	CGA Arg	GTT Val 660	Asp	GCT Ala	GAG Glu	GTA Val	GGG Gly 665	480
															CGC Arg	528
				Gly					Gly					Val	GCT Ala	576
ATG Met	TTA Leu	ATT Ile 700	Ser	CTA Leu	GCA Ala	AGT Ser	TCT Ser	Ala	GTT Val	AGT Ser	TCT Ser	GAA Glu 710	Asp	GGG Gly	GGT Gly	624

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Val	GCT Ala 715	CTT Leu	CGG Arg	AAA Lys	ATG Met	AGG Arg 720	GAA Glu	GTG Val	AAG Lys	Arg	GTA Val 725	CTC Leu	GAG Glu	CAG Gln	AGT Ser	6	572
												AGT Ser				7	720
ATT Ile	TCG Ser	AAA Lys	cGC Arg	TAT Tyr 750	TTG Leu	CAT His	TAT Tyr	GTC Val	TTT Phe 755	GCT Ala	GCG Ala	TGC Cys	GGT Gly	ACG Thr 760	ACC Thr	7	768
TTT Phe	GGT Gly	CGC Arg	GAG Glu 765	CTG Leu	TTG Leu	GAA Glu	ATA Ile	CGC Arg 770	CTG Leu	GGC Gly	AAA Lys	GCT Ala	TAT Tyr 775	CGA Arg	ATG Met	8	316
CTC Leu	TGT Cys	GCG Ala 780	GCG Ala	AGT Ser	gac Asp	TCG Ser	GGT Gly 785	GCT Ala	GTG Val	CTG Leu	AAG Lys	GTG Val 790	GCC Ala	ATG Met	TCC Ser	1	864
TCA Ser	GGT Gly 795	TTT Phe	TCG Ser	GAT Asp	TCA Ser	AGC Ser 800	CAT His	TTC Phe	AGC Ser	AAG Lys	AAA Lys 805	TTT Phe	AAG Lys	GAA Glu	AGA Arg		912
	GGT Gly											TGA					951
(2)	TAID	ORMA	TION	FOR	SEQ	ID	NO: :	24:									
(2)	TIME																
(2)	INE	(i) (.	A) L B) T	ENCE ENGT YPE: OPOL	H: 3	16 an no a	mino cid										
(2)	(ii	(i) (. ((A) L B) T D) T LECU	ENGT YPE:	H: 3 ami oGY: YPE:	16 am no a lin pro	mino cid ear tein	aci	ds	0: 2	4:						
	(ii (xi	(i) ((() MO) SE	A) L B) T D) T LECU QUEN	ENGT YPE: OPOL LE T CE D	H: 3 ami: OGY: YPE: ESCR	l6 am no a lin pro IPTI	mino cid ear tein ON:	aci SEQ	ds ID N	Ile		Ser	Glu	Gly	Ile		
Met 1	(ii (xi	(i) ((() MO) SE	A) L B) T D) T LECU QUEN	ENGT YPE: OPOL LE T CE D Arg 5	H: 3 ami OGY: YPE: ESCR	16 am no a lin pro pro IPTI	mino cid ear tein ON:	aci SEQ Met	ds ID N Ser 10	Ile	His			15 Gly			
Met 1 Thr	(ii (xi Thr	(i) (() MO) SE Thr	A) L B) T D) T LECU QUEN Ile Asp 20 His	ENGT YPE: OPOL LE T CE D Arg	H: 3 ami OGY: YPE: YPE: Trp Pro	l6 amno amno amno amno amno amno amno amno	mino cid ear tein ON: Arg	sEQ Met Trp 25	ds ID N Ser 10 Ala	Ile	His	Leu	Asn 30	15 Gly			
Met 1 Thr	(ii (xi Thr	(i) (i) (i) (i) MO) SE Thr Ala	A) L B) T D) T LECU QUEN Ile Asp 20	ENGT YPE: OPOL LE T CE D Arg S Ser	H: 3 ami: OGY: YPE: YPE: Trp Pro	16 amo according properties arguments arguments Leu val	mino cid ear tein ON: Arg His Gln 40	sEQ Met Trp 25	ID N Ser 10 Ala	Ile His	His Thr Arg	Leu Gly 45	Asn 30	15 Gly	Ser		

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DOVEDUBE TERBOO

Glu Ala Glu His Ser Tyr Leu Ile Gln Ile Arg Ser Gly Ala Leu Gly 85 90 95

Val Ala Ser Gly Gly Arg Lys Val Ile Leu Ala Asn Gly Asp Cys Ser $100 \hspace{1cm} 105 \hspace{1cm} 115 \hspace{1cm}$

Ile Val Asp Ser Arg Gln Asp Phe Thr Leu Ser Ser Asn Ser Ser Thr 115 \$120\$ \$125\$

Gln Gly Val Val Ile Arg Phe Pro Val Ser Trp Leu Gly Ala Trp Val 130 135

Ser Asn Pro Glu Asp Leu Ile Ala Arg Arg Val Asp Ala Glu Val Gly 145 150155155

Trp Gly Arg Ala Leu Ser Ala Ser Val Ser Asn Leu Asp Pro Leu Arg 165 170 175

Met Leu Ile Ser Leu Ala Ser Ser Ala Val Ser Ser Glu Asp Gly Gly 195 200 205

Val Ala Leu Arg Lys Met Arg Glu Val Lys Arg Val Leu Glu Gln Ser 210 215 220

Phe Ala Asp Ala Asn Leu Gly Pro Glu Ser Val Ser Ser Gln Leu Gly 225 230 235

Ile Ser Lys Arg Tyr Leu His Tyr Val Phe Ala Ala Cys Gly Thr Thr $245 \hspace{1.5cm} 250 \hspace{1.5cm} 250 \hspace{1.5cm} 255 \hspace{1.5cm}$

Phe Gly Arg Glu Leu Leu Glu Ile Arg Leu Gly Lys Ala Tyr Arg Met $260 \hspace{1.5cm} 265 \hspace{1.5cm} 270 \hspace{1.5cm}$

Leu Cys Ala Ala Ser Asp Ser Gly Ala Val Leu Lys Val Ala Met Ser 275 280 280

Ser Gly Phe Ser Asp Ser Ser His Phe Ser Lys Lys Phe Lys Glu Arg 290 295 300

Tyr Gly Val Ser Pro Val Ser Leu Val Arg Gln Ala 305 310 315

- (2) INFORMATION FOR SEQ ID NO: 25:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 735 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

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	(111)	HY)	POTH	ETIC	AL: 1	40										
	(iv)) AN	rı-sı	ENSE	: NO											
		(1)	A) Ni B) L(D) O'	AME/I DCAT: THER /gs	KEY: ION: INFO ene=	17: DRMA' "ecl	rion a"					l-Coi	4-ну∘	drata	ase"	
	AGC															48
Met	Ser	Pro	320	Leu	Asn	Arg	GIU	325	val	GIu	Val	Leu	330	Val	Leu	
	CAG															96
GIU	Gln	335	Ala	Asp	Ala	Arg	340	ьeu	vaı	Leu	Thr	345	Ата	GIĀ	GIU	
	TGG															144
ser	Trp 350	Thr	Ala	GIY	Met	355	Leu	гуs	GIu	Tyr	360	Arg	GIu	Thr	Asp	
	GGC															192
365	Gly	Pro	Glu	lle	370	GIn	GIu	Lys	He	Arg 375	Arg	GLu	Ala	Ser	380	
	CAG															240
Trp	Gln	Trp	Lys	Leu 385	Leu	Arg	Met	Tyr	Thr 390	Lys	Pro	Thr	Ile	Ala 395	Met	
	AAT															288
Val	Asn	Gly	Trp 400	Cys	Phe	Gly	Gly	Gly 405	Phe	Ser	Pro	Leu	Val 410	Ala	Cys	
GAT	CTG	GCC	ATC	TGT	GCC	GAC	GAG	GCC	ACC	TTT	GGC	CTG	TCC	GAG	ATC	336
Asp	Leu	Ala 415	Ile	Cys	Ala	Asp	Glu 420	Ala	Thr	Phe	Gly	Leu 425	Ser	Glu	Ile	
	TGG															384
Asn	Trp 430	Gly	Ile	Pro	Pro	Gly 435	Asn	Leu	Val	Ser	Lys 440	Ala	Met	Ala	Asp	
	GTG															432
Thr	Val	GLY	Hls	Arg	GLU	ser	ьeu	Tyr	Tyr	TTe	met	Thr	GLV	LVS	Thr	

TTT GGC GGT CAG CAG GCC GCC AAG ATG GGG CTT GTG AAC CAG AGT GTT Phe Gly Gly Gln Gln Ala Ala Lys Met Gly Leu Val Asn Gln Ser Val 465 475 480

450



			GAG Glu 480												CTG Leu	528
			AAC Asn												AAG Lys	576
			GAG Glu													624
			CAA Gln													672
			CAG Gln													720
	TAC Tyr		CGC Arg 560	TGA												735
	(ii)	I) I) I) IOM	EEQUE EECUI	ENGTH (PE: (POLO	H: 24 amir GY: PE:	44 am no ac line prot	mino cid ear ein	acio	ds	D: 26	5:					
Met 1			Thr									Leu	Glu	Val	Leu	
Glu	Gln	Asp	Ala 20	Asp	Ala	Arg	Val	Leu 25	Val	Leu	Thr	Gly	Ala 30	Gly	Glu	
Ser	Trp	Thr 35	Ala	Gly	Met	Asp	Leu 40	Lys	Glu	Tyr	Phe	Arg 45	Glu	Thr	Asp	
Ala	Gly 50	Pro	Glu	Ile	Leu	Gln 55	Glu	Lys	Ile	Arg	Arg 60	Glu	Ala	Ser	Thr	
Trp 65	Gln	Trp	Lys	Leu	Leu 70	Arg	Met	Tyr	Thr	Lys 75	Pro	Thr	Ile	Ala	Met 80	
Val	Asn	Gly	Trp	Cys 85	Phe	Gly	Gly	Gly	Phe 90	Ser	Pro	Leu	Val	Ala 95	Cys	
Asp	Leu	Ala	Ile 100	Cys	Ala	Asp	Glu	Ala 105	Thr	Phe	Gly	Leu	Ser	Glu	Ile	

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Asn Trp Gly Ile Pro Pro Gly Asn Leu Val Ser Lys Ala Met Ala Asp \$115\$ \$120\$ \$125\$

Thr Val Gly His Arg Glu Ser Leu Tyr Tyr Ile Met Thr Gly Lys Thr 130 135 140

Phe Gly Gly Gln Gln Ala Ala Lys Met Gly Leu Val Asn Gln Ser Val 145 \$150\$

Pro Leu Ala Glu Leu Arg Ser Val Thr Val Glu Leu Ala Gln Asn Leu 165 170 175

Arg Cys Arg Glu Leu Thr Trp Glu Gln Asn Glu Asp Tyr Leu Tyr Ala 195 200 205

Lys Leu Asp Gln Ser Arg Leu Leu Asp Pro Glu Gly Gly Arg Glu Gln 210 $$\rm 215$$

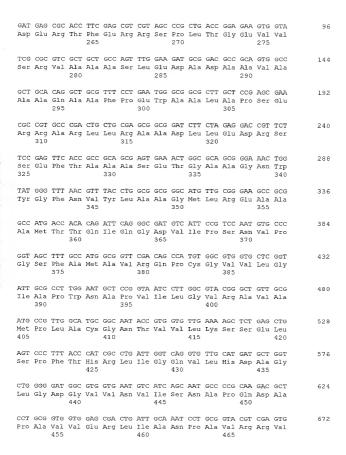
Gly Met Lys Gln Phe Leu Asp Glu Lys Ser Ile Lys Pro Gly Leu Gln 225 230 235 240

Thr Tyr Lys Arg

- (2) INFORMATION FOR SEQ ID NO: 27:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1446 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION:1..1443
 - (D) OTHER INFORMATION:/product= "Vanillin-Dehydrogenase" /gene= "vdh"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

ATG TTT CAC GTG CCC CTG CTT ATT GGT GGT AAG CCT TGT TCA GCA TCT Met Phe His Val Pro Leu Leu lle Gly Gly Lys Pro Cys Ser Ala Ser 245 \$250\$

48



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TTC n Phe 470								720
G CGT a Arg 5								768
C TTG e Leu								816
C TTT a Phe								864
r CTG g Leu								912
F AAG g Lys 550								960
C TTG l Leu 5								1008
GTC 1 Val								1056
C TTA / Leu								1104
A GAG								1152
TTG L Leu 630								1200
GAG Glu								1248
A ATG a Met								1296
A CCG								1344

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			TAC Tyr													1392
			CGC Arg													1440
ATC Ile 725	TAA															1446
(2)	INF	ORMA	TION	FOR	SEQ	ID 1	10: 2	28:								
		(2	SEQUI A) LI B) T	ENGTI (PE:	H: 48	31 ar no ac	mino cid									
			QUENO QUENO			-		SEQ :	ID N	o: 21	3:					
Met 1	Phe	His	Val	Pro 5	Leu	Leu	Ile	Gly	Gly 10	Lys	Pro	Cys	Ser	Ala 15	Ser	
Asp	Glu	Arg	Thr 20	Phe	Glu	Arg	Arg	Ser 25	Pro	Leu	Thr	Gly	Glu 30	Val	Val	
Ser	Arg	Val 35	Ala	Ala	Ala	Ser	Leu 40	Glu	Asp	Ala	Asp	Ala 45	Ala	Val	Ala	
Ala	Ala 50	Gln	Ala	Ala	Phe	Pro 55	Glu	Trp	Ala	Ala	Leu 60	Ala	Pro	Ser	Glu	
Arg 65	Arg	Ala	Arg	Leu	Leu 70	Arg	Ala	Ala	Asp	Leu 75	Leu	Glu	Asp	Arg	Ser 80	
Ser	Glu	Phe	Thr	Ala 85	Ala	Ala	Ser	Glu	Thr 90	Gly	Ala	Ala	Gly	Asn 95	Trp	
Tyr	Gly	Phe	Asn 100	Val	Tyr	Leu	Ala	Ala 105	Gly	Met	Leu	Arg	Glu 110	Ala	Ala	
Ala	Met	Thr 115	Thr	Gln	Ile	Gln	Gly 120	Asp	Val	Ile	Pro	Ser 125	Asn	Val	Pro	
Gly	Ser 130	Phe	Ala	Met	Ala	Val 135	Arg	Gln	Pro	Cys	Gly 140	Val	Val.	Leu	Gly	
Ile 145	Ala	Pro	Trp	Asn	Ala 150	Pro	Val	Ile	Leu	Gly 155	Val	Arg	Ala	Val	Ala 160	

Met Pro Leu Ala Cys Gly Asn Thr Val Val Leu Lys Ser Ser Glu Leu 165 170 175

Ser Pro Phe Thr His Arg Leu Ile Gly Gln Val Leu His Asp Ala Gly 180 185 190

Leu Gly Asp Gly Val Val Asn Val Ile Ser Asn Ala Pro Gln Asp Ala 195 200 205

Pro Ala Val Val Glu Arg Leu Ile Ala Asn Pro Ala Val Arg Arg Val 210 215 220

Asn Phe Thr Gly Ser Thr His Val Gly Arg Ile Ile Gly Glu Leu Ser 225 230 235 240

Ala Arg His Leu Lys Pro Ala Val Leu Glu Leu Gly Gly Lys Ala Pro 245 250 255

Phe Leu Val Leu Asp Asp Ala Asp Leu Asp Ala Ala Val Glu Ala Ala 260 265 270

Ala Phe Gly Ala Tyr Phe Asn Gln Gly Gln Ile Cys Met Ser Thr Glu 275 280 285

Arg Leu Ile Val Thr Ala Val Ala Asp Ala Phe Val Glu Lys Leu Ala 290 295 300

Arg Lys Val Ala Thr Leu Arg Ala Gly Asp Pro Asn Asp Pro Gln Ser 305 310 315 320

Val Leu Gly Ser Leu Ile Asp Ala Asn Ala Gly Gln Arg Ile Gln Val \$325\$ \$330\$ \$335

Leu Val Asp Asp Ala Leu Ala Lys Gly Ala Arg Gln Val Val Gly Gly 340 345 350

Gly Leu Asp Gly Ser Ile Met Gln Pro Met Leu Leu Asp Gln Val Thr 355 360 365

Glu Glu Met Arg Leu Tyr Arg Glu Glu Ser Phe Gly Pro Val Ala Val 370 \$375\$

Val Leu Arg Gly Asp Gly Asp Glu Glu Leu Leu Arg Leu Ala Asn Asp 385 390 395

Ser Glu Phe Gly Leu Ser Ala Ala Ile Phe Ser Arg Asp Val Ser Arg 405 \$410\$

Ala Met Glu Leu Ala Gln Arg Val Asp Ser Gly Ile Cys His Ile Asn 420 425 430

Gly Pro Thr Val His Asp Glu Ala Gln Met Pro Phe Gly Gly Val Lys 435 440 445

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			•														
Ser	Ser 450	Gly	Tyr	Gly	Ser	Phe 455	Gly	Ser	Arg	Ala	Ser 460	Ile	Glu	His	Phe		
Thr 465	Gln	Leu	Arg	Trp	Leu 470	Thr	Ile	Gln	Asn	Gly 475	Pro	Arg	His	Tyr	Pro 480		
Ile																	
(2)	INF	ORMA'	TION	FOR	SEQ	ID I	10:	29:									
	(i	() ()	A) L: B) T' C) S'	CE CI ENGTI YPE: TRANI OPOLO	H: 1 nuc: DEDNI	770 l leic Ess:	acio doul	pai. d	rs								
	(ii) Mo	LECU	LE T	PE:	DNA	(gei	nomi	c)								
	(iii) HY	POTH	ETIC	AL: 1	00											
	(iv) AN	ri-si	ENSE	: NO												
	(ix	(1	A) N	AME/F OCATI THER "F	ION: INFO	ll' DRMA	rion:		oduct Syntl		se"						
	(xi) SE	QUEN	CE DE	ESCRI	IPTI	ON: S	SEQ :	ID NO	o: 29	9:						
ATG	CGT	TCT	CTC	GAG	GCG	CTT	CTT	ccc	TTC	CCG	GGT	CGA	ATT	CTT	GAG		48
Met	Arg	Ser	Leu 485	Glu	Ala	Leu	Leu	Pro 490	Phe	Pro	Gly	Arg	Ile 495	Leu	Glu		
	CTC Leu																96
	AGG Arg 515															;	144
	CAC His															:	192
	GCA Ala															:	240

CTT CAG CTG GCA TTT GGG GCT ATG TAT GCG GGC ATT CCC TAT TGC CCG 288 Leu Gln Leu Ala Phe Gly Ala Met Tyr Ala Gly Ile Pro Tyr Cys Pro 565 570 GTG TCT CCT GCT TAT TCA CTG CTG TCG CAA GAT TTG GCG AAG CTG CGT 336 Val Ser Pro Ala Tyr Ser Leu Leu Ser Gln Asp Leu Ala Lys Leu Arg 580 585 CAC ATC GTA GGT CTT CTG CAA CCG GGA CTG GTC TTT GCT GCC GAT GCA 384 His Ile Val Gly Leu Leu Gln Pro Gly Leu Val Phe Ala Ala Asp Ala 595 600 GCA CCT TTC CAG CGC GCA ATT GAG ACC ATT CTG CCG GAC GAC GTG CCC 432 Ala Pro Phe Gln Arg Ala Ile Glu Thr Ile Leu Pro Asp Asp Val Pro 610 615 620 GCA ATC TTC ACT CGA GGC GAA TTG GCC GGG CGG CGC ACG GTG AGT TTT 480 Ala Ile Phe Thr Arg Gly Glu Leu Ala Gly Arg Arg Thr Val Ser Phe 630 GAC AGC CTG CTG GAG CAG CCT GGT GGG ATT GAG GCA GAT AAT GCC TTT 528 Asp Ser Leu Leu Glu Gln Pro Gly Gly Ile Glu Ala Asp Asn Ala Phe 650 GCG GCA ACT GGC CCC GAT ACG ATT GCC AAG TTC TTG TTC ACT TCT GGC 576 Ala Ala Thr Gly Pro Asp Thr Ile Ala Lys Phe Leu Phe Thr Ser Gly 665 TCT ACC AAA CTG CCT AAG GCG GTG CCG ACT ACT CAG CGA ATG CTC TGC 624 Ser Thr Lys Leu Pro Lys Ala Val Pro Thr Thr Gln Arg Met Leu Cys 675 GCC AAT CAG CAG ATG CTT CTG CAA ACT TTC CCG GTT TTT GGT GAA GAG 672 Ala Asn Gln Gln Met Leu Leu Gln Thr Phe Pro Val Phe Gly Glu Glu 690 695 700 CCG CCG GTG CTG GTG GAC TGG TTG CCG TGG AAC CAC ACC TTC GGC GGC 720 Pro Pro Val Leu Val Asp Trp Leu Pro Trp Asn His Thr Phe Gly Gly 710 AGC CAC AAC ATC GGC ATC GTG TTG TAC AAC GGC GGC ACG TAC TAC CTT 768 Ser His Asn Ile Gly Ile Val Leu Tyr Asn Gly Gly Thr Tyr Tyr Leu 725 730 735 GAC GAC GGT AAA CCA ACC GCC CAA GGG TTC GCC GAG ACG CTT CGC AAC 816 Asp Asp Gly Lys Pro Thr Ala Gln Gly Phe Ala Glu Thr Leu Arg Asn 740 745 TTG AGC GAA ATC TCT CCC ACT GCG TAC CTC ACT GTG CCG AAA GGC TGG 864 Leu Ser Glu Ile Ser Pro Thr Ala Tyr Leu Thr Val Pro Lys Gly Trp 760 GAG GAA TTA GTG GGT GCC CTT GAG CGA GAC AGT ACC CTG CGC GAA CGC 912 Glu Glu Leu Val Gly Ala Leu Glu Arg Asp Ser Thr Leu Arg Glu Arg 770 775 780

500 Ø g bath R N

)	
Ę	7
Ser.	
12	4
100	9
E	9
Africa,	1
0	
CO CO	-
8	
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E	
200	
0	-
CHUS	
C	7

										GCG Ala						9	60
CAA Gln	GGG	ATC Ile	TGG Trp 805	GAT Asp	CGT Arg	TTG Leu	GAC Asp	CGG Arg 810	GTC Val	GCT Ala	GAA Glu	CAG Gln	CAC His 815	TGT Cys	GGT Gly	10	08
										ATG Met						10	56
										ATG Met						11	04
										GTT Val 860						11	52
TTG Leu	GAA Glu	GGG Gly	CGT Arg	TTC Phe 870	CAT His	GGT Gly	CCG Pro	CAC His	GTC Val 875	ATG Met	AGC Ser	GGC Gly	TAC Tyr	TGG Trp 880	CGT Arg	12	00
										GAG Glu						12	48
										GCC Ala						12	96
										TTC Phe						13	44
										CGG Arg 940						139	92
										GCT Ala						14	40
										GAC Asp						148	88
GGG Gly																153	36

1770

			TGG				${\tt Trp}$					Asn				1584
	Gly		GCC Ala			Ile					Leu					1632
			GAT Asp		Gly					Lys					Gln	1680
CGC	GCT	GTT	TTG	CAA	TGG	CGG	TCG	GCG	AAA	GTT	GAT	GCG	CTG	TAT	CGT	1728

Arg Ala Val Leu Gln Trp Arg Ser Ala Lys Val Asp Ala Leu Tyr Arg 1045 1050 1055

GGT GAA GAT CAA TCC ATG CTG CGT GAC GAG GCC ACA CTG TGA
Gly Glu Asp Gln Ser Met Leu Arg Asp Glu Ala Thr Leu
1060 1065 1070

- (2) INFORMATION FOR SEQ ID NO: 30:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 589 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

Met Arg Ser Leu Glu Ala Leu Leu Pro Phe Pro Gly Arg Ile Leu Glu $1 \ \ \,$ 10 $15 \ \ \,$ 15

Arg Leu Glu His Trp Ala Lys Thr Arg Pro Glu Gln Thr Cys Val Ala $20 \\ 25 \\ 30$

Ala Arg Ala Ala Asn Gly Glu Trp Arg Arg Ile Ser Tyr Ala Glu Met 35 40 45

Phe His Asn Val Arg Ala Ile Ala Gln Ser Leu Leu Pro Tyr Gly Leu 50 60

Ser Ala Glu Arg Pro Leu Leu Ile Val Ser Gly Asn Asp Leu Glu His 65 70 75 80

Leu Gln Leu Ala Phe Gly Ala Met Tyr Ala Gly Ile Pro Tyr Cys Pro 85 $90\,$ 95

Val Ser Pro Ala Tyr Ser Leu Leu Ser Gln Asp Leu Ala Lys Leu Arg 100 105 110

His Ile Val Gly Leu Leu Gln Pro Gly Leu Val Phe Ala Ala Asp Ala 115 120 125 Ala Pro Phe Gln Arg Ala Ile Glu Thr Ile Leu Pro Asp Asp Val Pro 130 $$130\$

Ala Ile Phe Thr Arg Gly Glu Leu Ala Gly Arg Arg Thr Val Ser Phe 145 150 155 160

Asp Ser Leu Leu Glu Gln Pro Gly Gly Ile Glu Ala Asp Asn Ala Phe \$165\$

Ala Ala Thr Gly Pro Asp Thr Ile Ala Lys Phe Leu Phe Thr Ser Gly 180 $$180\$

Ser Thr Lys Leu Pro Lys Ala Val Pro Thr Thr Gln Arg Met Leu Cys 195 200

Ala Asn Gln Gln Met Leu Leu Gln Thr Phe Pro Val Phe Gly Glu Glu 210 215 220

Pro Pro Val Leu Val Asp Trp Leu Pro Trp Asn His Thr Phe Gly Gly 225 230 235

Ser His Asn Ile Gly Ile Val Leu Tyr Asn Gly Gly Thr Tyr Leu $245 \hspace{1cm} 250 \hspace{1cm} 255 \hspace{1cm}$

Asp Asp Gly Lys Pro Thr Ala Gln Gly Phe Ala Glu Thr Leu Arg Asn $260 \\ 265 \\ 270 \\$

Leu Ser Glu Ile Ser Pro Thr Ala Tyr Leu Thr Val Pro Lys Gly Trp \$275\$

Glu Glu Leu Val Gly Ala Leu Glu Arg Asp Ser Thr Leu Arg Glu Arg 290 295 300

Phe Phe Ala Arg Met Lys Leu Phe Phe Phe Ala Ala Ala Gly Leu Ser 305 310 315 320

Gln Gly Ile Trp Asp Arg Leu Asp Arg Val Ala Glu Gln His Cys Gly 325 330 335

Glu Arg Ile Arg Met Met Ala Gly Leu Gly Met Thr Glu Thr Ala Pro $340 \hspace{1.5cm} 345 \hspace{1.5cm} 350 \hspace{1.5cm}$

Ser Cys Thr Phe Thr Thr Gly Pro Leu Ser Met Ala Gly Tyr Ile Gly 355 360 365

Leu Pro Ala Pro Gly Cys Glu Val Lys Leu Val Pro Val Asp Gly Lys 370 375 380

Leu Glu Gly Arg Phe His Gly Pro His Val Met Ser Gly Tyr Trp Arg 385 $$ 390 $$ 395 $$ 400

Ala Pro Glu Gln Asn Ala Gln Ala Phe Asp Glu Glu Gly Tyr Tyr Cys 405 410 415

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Ser	Gly	Asp	Ala	Ile	Lys	Leu	Ala	Asp	Pro	Ala	Asp	Pro	Gln	Lys	Gly
			420					425					430		

- Leu Met Phe Asp Gly Arg Ile Ala Glu Asp Phe Lys Leu Ser Ser Gly $435 \ \ \, 440 \ \ \, 445$
- Val Phe Val Ser Val Gly Pro Leu Arg Thr Arg Ala Val Leu Glu Gly $450 \ \ \, 455 \ \ \, 460$
- Gly Ser Tyr Val Leu Asp Val Val Val Ala Ala Pro Asp Arg Glu Cys 465 \$470\$ 470 475
- Leu Gly Leu Leu Val Phe Pro Arg Leu Leu Asp Cys Arg Ala Leu Ser \$485\$
- Gly Leu Gly Lys Glu Ala Ser Asp Ala Glu Val Leu Ala Ser Glu Pro $500 \hspace{1.5cm} 505 \hspace{1.5cm} 510$
- Val Arg Ala Trp Phe Ala Asp Trp Leu Lys Arg Leu Asn Arg Glu Ala 515 520 525
- Thr Gly Asn Ala Ser Arg Ile Met Trp Val Gly Leu Leu Asp Thr Pro 530 535 540
- Arg Ala Val Leu Gln Trp Arg Ser Ala Lys Val Asp Ala Leu Tyr Arg 565 570 575
- Gly Glu Asp Gln Ser Met Leu Arg Asp Glu Ala Thr Leu
 580 585
- (2) INFORMATION FOR SEQ ID NO: 31:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1296 base pairs
 - (B) TYPE: nucleic acid (C) STRANDEDNESS: double
 - (C) STRANDEDNESS: GOUDI
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION:1..1293
 - (D) OTHER INFORMATION:/product= "beta-Ketothiolase"
 /gene= "aat"

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

										0. 0						
ATG Met 590	Ser	TGG	TCA Ser	GGG Gly	GGG Gly 595	Ala	TAC Tyr	TCG	GCG Ala	Phe 600	Ser	GAC Asp	ACT Thr	GCG Ala	TTG Leu 605	48
Val	Ala	Ala	. GTG Val	Arg 610	Thr	Pro	Trp	Ile	Asp 615	Cys	Gly	Gly	Ala	Leu 620	Ser	96
CTG Leu	GTG Val	TCG	CCT Pro 625	ATC Ile	GAC Asp	TTA Leu	GGG Gly	GTA Val 630	Lys	GTC Val	GCT Ala	CGC Arg	GAA Glu 635	GTT Val	CTG Leu	144
ATG Met	CGT Arg	GCG Ala 640	TCG Ser	CTT Leu	GAA Glu	CCA Pro	CAA Gln 645	ATG Met	GTC Val	GAT Asp	AGC Ser	GTA Val 650	CTC Leu	GCA Ala	GGC Gly	192
TCT	ATG Met 655	GCT Ala	CAA Gln	GCA Ala	AGC Ser	TTT Phe 660	GAT Asp	GCT Ala	TAC Tyr	CTG Leu	CTC Leu 665	CCG Pro	CGG Arg	CAC His	ATT Ile	240
GGC Gly 670	TTG Leu	TAC Tyr	AGC Ser	GGT Gly	GTT Val 675	CCC Pro	AAG Lys	TCG Ser	GTT Val	CCG Pro 680	GCC Ala	TTG Leu	GGG Gly	GTG Val	CAG Gln 685	288
CGC Arg	ATT Ile	TGC Cys	GGC Gly	ACA Thr 690	GGC Gly	TTC Phe	GAA Glu	CTG Leu	CTT Leu 695	CGG Arg	CAG Gln	GCC Ala	GGC Gly	GAG Glu 700	CAG Gln	336
			GGC Gly 705													384
			ccc Pro													432
GGT Gly	GCG Ala 735	CCC Pro	GTT Val	GAG Glu	TTC Phe	AAG Lys 740	GAT Asp	TTT Phe	TTG Leu	TGG Trp	GAG Glu 745	GCA Ala	TTG Leu	TTT Phe	GAT Asp	480
CCT Pro 750	GCT Ala	CCA Pro	GGA Gly	CTC Leu	GAC Asp 755	ATG Met	ATC Ile	GCT Ala	ACC Thr	GCA Ala 760	GAA Glu	AAC Asn	CTG Leu	GCG Ala	CGC Arg 765	528
CTG Leu	TAC Tyr	GGA Gly	ATC Ile	ACC Thr 770	AGG Arg	GGA Gly	GAA Glu	GCT Ala	AAT Asn 775	TCC Ser	TAC Tyr	GCG Ala	GTA Val	AGC Ser 780	AGC Ser	576
TTC Phe	GAG Glu	CGC Arg	GCA Ala 785	TTG Leu	AGG Arg	GCG Ala	Gln	GAG Glu 790	GAG Glu	AAA Lys	TGG Trp	ATT Ile	GAC Asp 795	CAA Gln	GAG Glu	624

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					ACG Thr												672
	rg .				CTG Leu												720
I.					GCA Ala												768
					GTG Val 850												816
					GCT Ala												864
					ATA Ile												912
	s				GGC Gly												960
	r				TTG Leu												1008
					GTT Val 930												1056
					ATT Ile												1104
					TTG Leu												1152
GC Al	a A	AAT Asn 975	AAC Asn	TTT Phe	CGA Arg	TAT Tyr	GGA Gly 980	ATT Ile	GCC Ala	TCG Ser	GCA Ala	TGC Cys 985	ATT Ile	GGT Gly	GGG Gly	GGA Gly	1200
	n (GTT Val							Phe					1248
					ATG Met 1010	Ile					His)	1293

TAA

1296

INFORMATION			

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 431 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

Met Ser Trp Ser Gly Gly Ala Tyr Ser Ala Phe Ser Asp Thr Ala Leu $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15$

Val Ala Ala Val Arg Thr Pro Trp Ile Asp Cys Gly Gly Ala Leu Ser

Leu Val Ser Pro Ile Asp Leu Gly Val Lys Val Ala Arg Glu Val Leu 35 40 45

Ser Met Ala Gln Ala Ser Phe Asp Ala Tyr Leu Leu Pro Arg His Ile 65 70 75 80

Gly Leu Tyr Ser Gly Val Pro Lys Ser Val Pro Ala Leu Gly Val Gln 85 90 95

Ile Ser Gln Gly Ala Asp His Val Leu Cys Val Ala Ala Glu Ser Met 115 \$120\$

Ser Arg Asn Pro Ile Ala Ser Tyr Thr His Arg Gly Gly Phe Arg Leu 130 $$135\$

Gly Ala Pro Val Glu Phe Lys Asp Phe Leu Trp Glu Ala Leu Phe Asp 145 150 155 160

Pro Ala Pro Gly Leu Asp Met Ile Ala Thr Ala Glu Asn Leu Ala Arg 165 170 175

Leu Tyr Gly Ile Thr Arg Gly Glu Ala Asn Ser Tyr Ala Val Ser Ser 180 185 190

Phe Glu Arg Ala Leu Arg Ala Gln Glu Glu Lys Trp Ile Asp Gln Glu 195 200 205

Ile Val Ala Val Thr Asp Glu Gln Phe Asp Leu Glu Gly Tyr Asn Ser 210 215 220 - 100 -

Arg Ala Ile Glu Leu Pro Arg Lys Ala Lys Leu Leu Ile Val Thr Val

Ile Arg Gly Leu Ala Val Phe Glu Ala Leu Ser Arg Leu Lys Pro Val 250

His Ser Gly Gly Val Gln Thr Ala Gly Asn Ser Cys Ala Val Val Asp 260 265

Gly Ala Ala Ala Leu Val Ala Arg Glu Ser Ser Ala Thr Gln Pro 280 285

Val Leu Ala Arg Ile Leu Ala Thr Ser Val Val Gly Ile Glu Pro Glu 295

His Met Gly Leu Gly Pro Ala Pro Ala Ile Arg Leu Leu Leu Ala Arg 305 310 315

Ser Asp Leu Ser Leu Arg Asp Ile Asp Leu Phe Glu Ile Asn Glu Ala 330

Gln Ala Ala Gln Val Leu Ala Val Gln His Glu Leu Gly Ile Glu His 340 345 350

Ser Lys Leu Asn Ile Trp Gly Gly Ala Ile Ala Leu Gly His Pro Leu 355

Ala Ala Thr Gly Leu Arg Leu Cys Met Thr Leu Ala His Gln Leu Gln

Ala Asn Asn Phe Arg Tyr Gly Ile Ala Ser Ala Cys Ile Gly Gly Gly 385 390 395

Gln Gly Met Ala Val Leu Leu Glu Asn Pro His Phe Gly Ser Ser Ser 405 410

Ala Arg Ser Ser Met Ile Asn Arg Val Asp His Tyr Pro Leu Ser 420 425 430

- (2) INFORMATION FOR SEQ ID NO: 33:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1596 base pairs (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double

 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

(ix) FEATURE:

595

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			(B) L	OCAT THER	ION:	11	593 TION	:/pr	oduc	t= "	Chem	otax	is-P	rote	in"	
	(xi	.) SE	QUEN	CE D	ESCR	IPTI	ON:	SEQ	ID N	o: 3	3:					
ATG Met	ATT	AGT Ser	TTC Phe 435	GCT Ala	CGT Arg	ATG Met	GCA Ala	GAA Glu 440	Ser	TTA Leu	GGA Gly	GTC Val	CAG Gln 445	GCT Ala	AAA Lys	48
CTT	GCC Ala	CTT Leu 450	GCC Ala	TTC Phe	GCA Ala	CTC Leu	GTA Val 455	TTA Leu	TGT Cys	GTC Val	GGG Gly	CTG Leu 460	Ile	GTT Val	ACC Thr	96
GGC	ACG Thr 465	Gly	TTC Phe	TAC Tyr	AGT Ser	GTA Val 470	CAT His	ACC Thr	TTG Leu	TCA Ser	GGG Gly 475	TTG Leu	GTG Val	GAA Glu	AAG Lys	144
AGC Ser 480	GCG Ala	ATA	GCT Ala	GGT Gly	GAG Glu 485	TTG Leu	CGG Arg	GCG Ala	AAA Lys	ATT Ile 490	CAG Gln	GAA Glu	CTG Leu	AAG Lys	GTT Val 495	192
CTG Leu	GAG Glu	CAG Gln	CGC Arg	GCC Ala 500	TTA Leu	TTC Phe	ATC Ile	GCC Ala	GAT Asp 505	GAA Glu	GGG Gly	TCG Ser	CTG Leu	AAG Lys 510	CAG Gln	240
CGC Arg	TCG Ser	ATC Ile	CTC Leu 515	CTA Leu	AGT Ser	CAG Gln	GTG Val	ATA Ile 520	GCT Ala	GAA Glu	GTT Val	AAT Asn	GAT Asp 525	GCT Ala	ATA Ile	288
GAT Asp	ATT Ile	TTT Phe 530	GAC Asp	TTT Phe	CAG Gln	CGC Arg	GGA Gly 535	CGA Arg	TCT Ser	GAG Glu	TTA Leu	CTT Leu 540	AAA Lys	TTC Phe	GCT Ala	336
GCT Ala	TCT Ser 545	TCG Ser	CGC Arg	GAA Glu	GCA Ala	AGT Ser 550	TAC Tyr	TCC Ser	ATT Ile	GAG Glu	GTC Val 555	GGT Gly	AGT Ser	AAC Asn	GCT Ala	384
GCG Ala 560	GCC Ala	GAT Asp	AAG Lys	TTG Leu	CAG Gln 565	TCG Ser	GGC Gly	GAA Glu	CCA Pro	AGT Ser 570	GAC Asp	GCA Ala	TTG Leu	ATG Met	GTT Val 575	432
GCC Ala	GAT Asp	AAA Lys	AAG Lys	CTG Leu 580	AAT Asn	GTT Val	GAG Glu	TAT Tyr	GAG Glu 585	CAA Gln	TTG Leu	AGT Ser	TCT Ser	GCT Ala 590	GTG Val	480
AAT Asn	GCA Ala	CTG Leu	ATG Met	GGG Gly	CAT His	TTA Leu	ATT Ile	GAG Glu	GAT Asp	CAG Gln	AAT Asn	GAA Glu	AAA Lys	GTT Val	CCA Pro	528

600

605

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												ACG Thr 620				5	76
												GTT Val				6	24
												GGC Gly				6	72
												CAG Gln				7	20
												GTC Val				7	68
												GAC Asp 700				8	16
												AAG Lys				8	64
												ACC Thr				9	12
												GTC Val				9	60
GAA Glu	AAG Lys	GCA Ala	CGC Arg 755	GGT Gly	GGT Gly	GAA Glu	AGT Ser	GTC Val 760	GTT Val	AAC Asn	AAG Lys	GCC Ala	GTT Val 765	gat Asp	TTC Phe	10	8 0
												GAC Asp 780				10	56
												GTA Val				11	04
												AAT Asn				11	52
												GCG Ala				12	00

8.00

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			ATG Met					1248
			TTG Leu 855					1296
			GTC Val					1344
			GCT Ala					1392
			CAG Gln					1440
			AAC Asn					1488
			AAA Lys 935					1536
			AGT Ser					1584
CAG Gln	TAG							1596

- (2) INFORMATION FOR SEQ ID NO: 34:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 531 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

Met Ile Ser Phe Ala Arg Met Ala Glu Ser Leu Gly Val Gln Ala Lys $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Leu Ala Leu Ala Phe Ala Leu Val Leu Cys Val Gly Leu Ile Val Thr $20 \\ 25 \\ 30$

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Gly Thr Gly Phe Tyr Ser Val His Thr Leu Ser Gly Leu Val Glu Lys 35 40 Ser Ala Ile Ala Gly Glu Leu Arg Ala Lys Ile Gln Glu Leu Lys Val Leu Glu Gln Arg Ala Leu Phe Ile Ala Asp Glu Gly Ser Leu Lys Gln Arg Ser Ile Leu Leu Ser Gln Val Ile Ala Glu Val Asn Asp Ala Ile Asp Ile Phe Asp Phe Gln Arg Glv Arg Ser Glu Leu Leu Lvs Phe Ala 100 105 Ala Ser Ser Arg Glu Ala Ser Tyr Ser Ile Glu Val Gly Ser Asn Ala 120 Ala Ala Asp Lys Leu Gln Ser Gly Glu Pro Ser Asp Ala Leu Met Val Ala Asp Lys Lys Leu Asn Val Glu Tyr Glu Gln Leu Ser Ser Ala Val 150 155 Asn Ala Leu Met Gly His Leu Ile Glu Asp Gln Asn Glu Lys Val Pro 165 170 Leu Ile Tyr Tyr Met Leu Gly Gly Val Thr Leu Phe Thr Met Leu Met 185 Ser Ala Tyr Ser Val Trp Phe Ile Ser Arg Gln Leu Val Pro Pro Leu 200 Lys Ser Thr Val Gln Leu Ala Glu Arg Ile Ala Ser Gly Asp Leu Ala 210 Asp Val Gly Asp Ser Arg Arg Lys Asp Glu Ile Gly Gln Leu Gln Ser 235 Ala Thr Arg Arg Met Ala Ile Gly Leu Arg Asn Leu Val Gly Asp Ile 245 Gly Gln Ser Arg Ala Gln Leu Val Ser Ser Ser Ser Asp Leu Ser Ala Ile Cys Ala Gln Ala Gln Ile Asp Val Glu Cys Gln Lys Leu Ser Val 280 Ala Gln Val Ser Thr Ala Val Asn Glu Leu Val Glu Thr Val Gln Ala 290 295

315

Ile Ala Lys Ser Thr Glu Glu Ala Ala Thr Val Ala Val Leu Ala Asp 305

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Glu Lys Ala Arg Gly Gly Glu Ser Val Val Asn Lys Ala Val Asp Phe \$325\$ \$330\$

Ile Glu His Leu Ser Gly Asp Met Ala Glu Leu Gly Asp Ala Met Glu $340 \hspace{1.5cm} 345 \hspace{1.5cm} 350 \hspace{1.5cm}$

Arg Leu Gln Asn Asp Ser Ala Gln Ile Asn Lys Val Val Asp Val Ile 355 360 365

Lys Ala Val Ala Glu Gln Thr Asn Leu Leu Ala Leu Asn Ala Ala Ile 370 375 380

Glu Ala Ala Arg Ala Gly Glu Gln Gly Arg Gly Phe Ala Val Val Ala 385 \$390\$ 395 400

Asp Glu Val Arg Ala Leu Ala Met Arg Thr Gln Gln Ser Thr Lys Glu 405 410 415

Ile Glu Arg Leu Val Val Ser Leu Gln Gln Gly Ser Glu Ala Ala Gly 420 425 430

Glu Leu Met Arg Arg Gly Lys Val Arg Thr His Asp Val Val Gly Leu 435 440 445

Ala Gln Gln Ala Ala Arg Arg Ala Thr Arg Asn Tyr Pro Ala Val Ala $450 \hspace{1.5cm} 455 \hspace{1.5cm} 460 \hspace{1.5cm}$

Gly Ile Gln Ala Met Asn Tyr Gln Ile Ala Ala Gly Ala Glu Gln Gln 465 \$470\$

Gly Ala Ala Val Val Gln Ile Asn Gln Asn Met Leu Glu Val His Lys 485 490 495

Met Ala Asp Glu Ser Ala Ile Lys Ala Gly Gln Thr Met Lys Ser Ser 500 505 510

Lys Glu Leu Ala His Leu Gly Ser Ala Leu Gln Lys Ser Val Asp Arg 515 520 525

Phe Gln Leu 530

- (2) INFORMATION FOR SEQ ID NO: 35:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 411 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

	(ix	(1	A) N	AME/I OCAT: THER "T:	ION:	comp DRMA' krip	TION tion:	:/pr	44 oduc gula		Prot	ein"					
	(xi) SE	QUEN	CE D	ESCR:	[PTI	ON:	SEQ :	ID N	o: 3	5:						
CTA	GCCT.	AAC '	rgtt:	GCGC'	TT C	AGGC'	rccg	CAT	GGAT(CTTG	TGC	AGCA	GCA .	ATAG	CAAT	rg	6
TTC	ACGT!	rcg :	rcat:	CACT	CA G	CATC	GACG'	r cg	CGTC'	rtgg	TCG	CTCT	GTA	CCAC	SATC:	ГT	12
CTT	CAGC!	rcr :	TTGA:	SCTG	CG T	CTCC	CCAG	C TT	rgct	GAGA	AAT	ATCC	CAT	AGGA <i>I</i>	ACGC!	ГT	18
GTC	CGGC'	TTG (CAGC	GCAC	GC G	CACA	GCAA)	G GC	CGAG	CTTC	TCG	AGCT	rgt '	TCAG	CAAG	GG	24
AAC	CAGT'	rgr (GGTG	GTTC	GA T	rgcg	AGCA'	r cc	GCGC'	ragg	TCA	CCT	GCA '	TAAG	CCA	GG	30
GCT	CGCT	rcg 2	ATGA!	rtag:	AA G	rgcc	GACA(G CT	GCGC	CGGG	CGT	AGGT	CAT :	ATGG	CGTC	AG	36
GGC.	TCA	ATC 2	AGGC	CCTG	AG C	GAGC'	FTCA	G CT	GTGA	GCCG	GCG'	raag	GCA '	T			41
(2)		(i) : (i) (i)	SEQUI A) Li 3) Ti	FOR ENCE ENGTI YPE: OPOLO	CHAI H: 13	RACTI 36 an	ERIS mino cid	rics									
				LE T				SEQ :	ID N	D: 36	5:						
Met 1	Pro	Tyr	Ala	Gly 5	Ser	Gln	Leu	Lys	Leu 10	Ala	Gln	Gly	Leu	Ile 15	Glu		
Ala	Leu	Thr	Pro 20	Tyr	Asp	Leu	Arg	Pro 25	Ala	Gln	Leu	Ser	Ala 30	Leu	Leu		
Ile	Ile	Glu 35	Ala	Ser	Pro	Gly	Leu 40	Met	Gln	Ala	Asp	Leu 45	Ala	Arg	Met		
Leu	Ala 50	Ile	Glu	Pro	Pro	Gln 55	Leu	Val	Pro	Leu	Leu 60	Asn	Lys	Leu	Glu		
Lys 65	Leu	Gly	Leu	Ala	Val 70	Arg	Val	Arg	Cys	Lys 75	Pro	Asp	Lys	Arg	Ser 80		

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Lys	Lys	Ile	Val 100	Va1	Gln	Ser	Asp	G1n 105	Asp	Ala	Thr	Ser	Met 110	Leu	Ser	
Asp	Asp	Glu 115	Arg	Glu	Gln	Leu	Leu 120	Leu	Leu	Leu	His	Lys 125	Ile	His	Ala	
Glu	Pro 130	Glu	Ala	Gln	Gln	Leu 135	Gly									
(2)	INFO	ORMAT	ION	FOR	SEQ	ID 1	10: 3	37:								
	(i)	(E		NGTH PE: RANI	: 14 nucl	146 l eic ESS:	ase acio doul	pai:	rs							
	(ii	MOI	ECUI	E TY	PE:	DNA	(ge	nomi	=)							
	(iii)	HYE	POTHE	TICA	AL: N	10										
	(iv	NA (I-SE	NSE:	NO											
		(E	A) NA B) Lo D) OT	AME/H DCATI THER "Co /ge	ION: INFO onife	DRMA eryla "ca:	TION alde ldh"	:/pro hyd-1 SEQ :	Dehy	droge		e"				
	AGC Ser															48
Met	ser	TTE	140	GIĀ	Leu	ASII	сту	145	PLO	Val	GIY	ALG	150	GIII	Бей	
	TCG Ser															96
	AAC Asn 170															144
	CTG Leu															192
	AAT Asn									Cys						240

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GTG Val	GCA Ala	AGC Ser	CTG Leu 220	AAG Lys	GAT Asp	AGC Ser	CGC Arg	GAG Glu 225	His	GTG Val	GCC	AAA Lys	TGG Trp 230	ATG Met	GAG Glu	288
CCC Pro	GAA Glu	CAT His 235	CAC His	AAG Lys	GCG Ala	ATG Met	TTT Phe 240	CCA Pro	GGG Gly	GCG Ala	GAG Glu	GCA Ala 245	CGC Arg	GTT Val	GAG Glu	336
TTT	CAG Gln 250	Pro	CTG Leu	GGT Gly	GTC Val	GTT Val 255	GGG Gly	GTC Val	ATT	AGT Ser	CCC Pro 260	Trp	AAC Asn	TTC Phe	CCT Pro	384
ATC Ile 265	GTA Val	CTG Leu	GCC Ala	TTT Phe	GGG Gly 270	CCG Pro	CTG Leu	GCC Ala	GGC Gly	ATA Ile 275	TTC Phe	GCA Ala	GCA Ala	GGT Gly	AAT Asn 280	432
Arg	Ala	Met	CTC Leu	Lys 285	Pro	Ser	Glu	Leu	Thr 290	Pro	Arg	Thr	Ser	Ala 295	Leu	480
Leu	Ala	Glu	CTA Leu 300	Ile	Ala	Arg	Tyr	Phe 305	Asp	Glu	Thr	Glu	Leu 310	Thr	Thr	528
Val	Leu	Gly 315	GAC Asp	Ala	Glu	Val	Gly 320	Ala	Leu	Phe	Ser	Ala 325	Gln	Pro	Phe	576
Asp	His 330	Leu	ATC Ile	Phe	Thr	Gly 335	Gly	Thr	Ala	Val	Ala 340	Lys	His	Ile	Met	624
Arg 345	Ala	Ala	GCG Ala	Asp	Asn 350	Leu	Val	Pro	Val	Thr 355	Leu	Glu	Leu	Gly	Gly 360	672
AAA Lys	TCG Ser	CCG Pro	GTG Val	ATC Ile 365	GTT Val	TCC Ser	CGC Arg	AGT Ser	GCA Ala 370	GAT Asp	ATG Met	GCG Ala	GAC Asp	GTT Val 375	GCA Ala	720
CAA Gln	CGG Arg	GTG Val	TTG Leu 380	ACG Thr	GTG Val	AAA Lys	ACC Thr	TTC Phe 385	AAT Asn	GCC Ala	GGG Gly	CAA Gln	ATC Ile 390	TGT Cys	CTG Leu	768
GCA Ala	CCG Pro	GAC Asp 395	TAT Tyr	GTG Val	CTG Leu	Leu	CCG Pro 400	GAA Glu	GAA Glu	TCG Ser	CTG Leu	GAT Asp 405	AGC Ser	TTT Phe	GTC Val	816
Ala	GAG Glu 410	GCG Ala	ACG Thr	CGC Arg	TTC Phe	GTG Val 415	GCC Ala	GCA Ala	ATG Met	TAT Tyr	CCC Pro 420	TCG Ser	CTT Leu	CTA Leu	GAT Asp	864
AAT Asn 425	CCG Pro	GAT Asp	TAC . Tyr	Thr	TCG Ser 430	ATC Ile	ATC Ile	AAT Asn	GCC Ala	CGA Arg 435	AAT Asn	TTC Phe	GAC Asp	CGT Arg	CTG Leu 440	912

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						AAG Lys 450					960
						GAT Asp				:	1008
						GAT Asp				:	1056
		 		-		ATC Ile					1104
						AAG Lys				;	1152
						CGT Arg 530					1200
						GAT Asp					1248
						GGG Gly			GCA Ala		1296
						TTC Phe					1344
						AAC Asn					1392
						TCT Ser 610					1440
TGT Cys	TAG										1446

- (2) INFORMATION FOR SEQ ID NO: 38:
 - (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 481 amino acids

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- (B) TYPE: amino acid (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

Met Ser Ile Leu Gly Leu Asn Gly Ala Pro Val Gly Ala Glu Gln Leu $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15$

Gly Ser Ala Leu Asp Arg Met Lys Lys Ala His Leu Glu Gln Gly Pro \$20\$

Ala Asn Leu Glu Leu Arg Leu Ser Arg Leu Asp Arg Ala Ile Ala Met 35 40 45

Leu Leu Glu Asn Arg Glu Ala Ile Ala Asp Ala Val Ser Ala Asp Phe 50 60

Gly Asn Arg Ser Arg Glu Gln Thr Leu Leu Cys Asp Ile Ala Gly Ser 65 70 75 80

Val Ala Ser Leu Lys Asp Ser Arg Glu His Val Ala Lys Trp Met Glu $85 \hspace{1cm} 90 \hspace{1cm} 95$

Pro Glu His His Lys Ala Met Phe Pro Gly Ala Glu Ala Arg Val Glu 100 105 110

Phe Gln Pro Leu Gly Val Val Gly Val Ile Ser Pro Trp Asn Phe Pro 115 120 125

Ile Val Leu Ala Phe Gly Pro Leu Ala Gly Ile Phe Ala Ala Gly Asn 130 \$135\$

Arg Ala Met Leu Lys Pro Ser Glu Leu Thr Pro Arg Thr Ser Ala Leu 145 150 150 155

Leu Ala Glu Leu Ile Ala Arg Tyr Phe Asp Glu Thr Glu Leu Thr Thr 165 170 175

Val Leu Gly Asp Ala Glu Val Gly Ala Leu Phe Ser Ala Gln Pro Phe 180 185 190

Asp His Leu Ile Phe Thr Gly Gly Thr Ala Val Ala Lys His Ile Met 195 \$200\$

Arg Ala Ala Asp Asn Leu Val Pro Val Thr Leu Glu Leu Gly Gly 210 215 220

Lys Ser Pro Val Ile Val Ser Arg Ser Ala Asp Met Ala Asp Val Ala 225 230 235

Gln Arg Val Leu Thr Val Lys Thr Phe Asn Ala Gly Gln Ile Cys Leu $245 \hspace{1.5cm} 255 \hspace{1.5cm}$

400

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Ala Glu Ala Thr Arg Phe Val Ala Ala Met Tyr Pro Ser Leu Leu Asp 275 280 285

Asn Pro Asp Tyr Thr Ser Ile Ile Asn Ala Arg Asn Phe Asp Arg Leu $290 \\ \hspace{1.5cm} 295 \\ \hspace{1.5cm} 300 \\ \hspace{1.5cm}$

His Arg Tyr Leu Thr Asp Ala Gln Ala Lys Gly Gly Arg Val Ile Glu 305 \$310\$ 315 320

Ile Asn Pro Ala Ala Glu Glu Leu Gly Asp Ser Gly Ile Arg Lys Ile \$325\$

Ala Pro Thr Leu Ile Val Asn Val Ser Asp Glu Met Leu Val Leu Asn 340 345 350

Glu Glu Ile Phe Gly Pro Leu Leu Pro Ile Lys Thr Tyr Arg Asp Phe 355 360 365

Asp Ser Ala Ile Asp Tyr Val Asn Ser Lys Gln Arg Pro Leu Ala Ser 370 \$375\$

Tyr Phe Phe Gly Glu Asp Ala Val Glu Arg Glu Gln Val Leu Lys Arg 385 $$ 390 $$ 395 $$ 400

Thr Val Ser Gly Ala Val Val Val Asn Asp Val Met Ser His Val Met 405 410 415

Met Asp Thr Leu Pro Phe Gly Gly Val Gly His Ser Gly Met Gly Ala 420 425 430

Tyr His Gly Ile Tyr Gly Phe Arg Thr Phe Ser His Ala Lys Pro Val 435 440 445

Leu Val Gln Ser Pro Val Gly Glu Ser Asn Leu Ala Met Arg Ala Pro $450 \ \ \, 455 \ \ \, 460$

Tyr Gly Glu Ala Ile His Gly Leu Leu Ser Val Leu Leu Ser Thr Glu 465 \$470\$

Cys

- (2) INFORMATION FOR SEQ ID NO: 39:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1827 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

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(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(ix) FEATURE:

400

(A) NAME/KEY: CDS

(B) LOCATION: complement (4..1827)

(D) OTHER INFORMATION:/product=

"Transkriptions-Aktivator-Protein" /gene= "tap"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

CTATTTGTCT AGTGGTCGGC GCGAAATTCG ATAAGAAAGC TGGGCGCGAG TGAGGCCGAG 60 CCGCCGGCA GCTTCCGAGA CATTGCCTTT CACCTGGCCC AGAGCATGGC TAATCATCGC 120 GTCCTCCACT TCTTGCAGCG TCATCGCGCT CAGGTCCTTT GAGTCAAGCG GCGAGTCGAT 180 TGTGCTGGTC GGTTTGGAGA AGGAAGTACT TGGGCTGCCA GTTTCCTGTG GCTGATTATC 240 TTGAGCGGTG GCCAGGATGC CGCTGGCCCC AATGGAGAAC ATCGGTTGAG TCAGTCGTTC 300 ACCGCTAGTG AAGAGGTGGC TCACGTCAAT GGCTCCATCC TCCGGAGCGC TGATGACTCC 360 GCGCTCCACC AAATTTTGAA GCTCCCGGAT GTTTCCTGGA AAGTCGTAGC CAAGCAGGGC 420 ATTGGCTGCA CGTGGAGTGA ATCCGCTGAC CACCCGGCTA TGACGCTGAT TGAAGCGGTG 480 CAGGAAATAG GTCATCAGGA GGGGAATGTC TTCCTTCCTC TCTCGAAGCG GCGGGAGGTG 540 GATCGGGTAA ACATTGAGGC GGAAAAAAAG GTCCTCGCGG AACTCGCCGC GCTGGACGCC 600 TGCGCGAAGA TCGACATTGG TTGCGGCTAC CACACGGACG TCAACCTTGA GTGTCCTGCT 660 TCCGCCAACC CGTTCGACCT CCGACTCTTG CAGGGCGCGA AGTAACTTCC CTTGGGCCAC 720 GAGGCTTAGC GTCCCTATCT CGTCAAGGAA TAGTGTGCCG CCCGAAGCGC GCTCGAACCG 780 TCCTGCTCGA GATTGGGTGG CGCCGGTAAA CGCCCCCGT TCGACGCCGA ACAACTCGGA 840 CTCCATCAGG GTTTCGGGAA TACGTGCGCA ATTGACCGCA ACAAACGGGC CGTCGTGTCT 900 GGGGCTGATG CGGTGAAGCA TGCGGGCGAA CATCTCCTTG CCCACACCTG ATTCACCCGT 960 AAACAGTACC GTCGCCTCCG TGGGTGCTAC GCGCTTCAGC ATGTGGCAGG CAGCATTGAA 1020 TGCCGAGGAA ATTCCCACCA TGTCGTGTTC CGATGCAGTG CTTGAGTCTG CGGCGGAGTG 1080 ATGGGGAGTG TTCCTTTGTC CCTGCTGCGT TCTTCGTCTC TGCGGCGTGC TTGGTTGCCG 1140 ACAAATGGTT GCGCTAAGCG CCGCCAAGTC CTCTTCGGCG TCTTCCCATT CTTCCGCTGG 1200 500

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CTTGCCGATC	ATGCGGCAGA	TCTGCGAACC	CGTGGAGCGG	CATTCCACCT	CTCGGTAAAG	1260
GATGAGGCG#	CCAACCAGCG	CGGACGTATA	GCCAATGGCA	TAACCCGTCT	GCGTCCAGCA	1320
CGCGGGCTCG	GTGCCGATGC	CGTAGTGCGC	AATATGTTCA	TCATCTTCGC	TCGAATGGTG	1380
CCAGAGGAAT	TCGCCGTAGT	AGGTCCCCAA	ATCCATGTCG	AAGTCGAAGT	GGATCGGCTC	1440
CACGCGTACT	GCGCCTTCCA	GAGAGTGCAA	GTTCGGGCCG	GCGGCAAATA	GGGAGAGCGG	1500
ATCGGCGTTG	CTGAAGCGCT	CCTTCAGAAG	GGCGGCATCT	TTGGCGCCGC	AGTGGTAACC	1560
GTTCGCAGC	ATGATTCCGC	GGGCGCGGGC	GAAGCCCACG	CTTTCAATTA	ATTCGCGTCG	1620
CAATGCACCC	AGTCCGCTGC	TGTGGAGGAG	CAGCATTCGC	GCGCCGTTCA	ACCAGATGCG	1680
PCCATCGCCA	GGGCTGAAAA	GGAGGGATTC	AGTGAGGTCA	TGAAGGGAGG	GGACGGCGCC	1740
rggctccaat	TGCTCGATGG	CGCCGCGATT	GAGTGTCTTG	GGCGCGGTCT	TGGAGAGTTC	1800
GGCTAGGGAG	ATAAATTTGC	TGGCCAT				1827

- (2) INFORMATION FOR SEQ ID NO: 40:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 608 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:
- Lys Thr Leu Asn Arg Gly Ala Ile Glu Glu Elu Glu Pro Gly Ala Val $20 \hspace{1.5cm} 25 \hspace{1.5cm} 30$
- Pro Ser Leu His Asp Leu Thr Glu Ser Leu Leu Phe Ser Pro Gly Asp $35 \ \ \, 40 \ \ \, 45$
- Gly Arg Ile Trp Leu Asn Gly Ala Arg Met Leu Leu Leu His Ser Ser 50 60
- Gly Leu Gly Ala Leu Arg Arg Glu Leu Ile Glu Ser Val Gly Phe Ala 65 70 75 80
- Arg Ala Arg Gly Ile Met Leu Arg Thr Gly Tyr His Cys Gly Ala Lys $85 \hspace{1cm} 90 \hspace{1cm} 95$
- Asp Ala Ala Leu Leu Lys Glu Arg Phe Ser Asn Ala Asp Pro Leu Ser 100 105 110

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Leu	Phe	Ala 115	Ala	Gly	Pro	Asn	Leu 120	His	Ser	Leu	Glu	Gly 125	Ala	Val	Arg
Val	Glu 130	Pro	Ile	His	Phe	Asp 135	Phe	Asp	Met	Asp	Leu 140	Gly	Thr	Tyr	Tyr
Gly 145	Glu	Phe	Leu	Trp	His 150	His	Ser	Ser	Glu	Asp 155	Asp	Glu	His	Ile	Ala 160
His	Tyr	Gly	Ile	Gly 165	Thr	G1u	Pro	Ala	Cys 170	Trp	Thr	Gln	Thr	Gly 175	Tyr
Ala	Ile	Gly	Tyr 180	Thr	Ser	Ala	Leu	Val 185	Gly	Arg	Leu	Ile	Leu 190	Tyr	Arg
Glu	Val	Glu 195	Cys	Arg	Ser	Thr	Gly 200	Ser	Gln	Ile	Cys	Arg 205	Met	Ile	Gly
Lys	Pro 210	Ala	Glu	Glu	Trp	Glu 215	Asp	Ala	Glu	Glu	Asp 220	Leu	Ala	Ala	Leu
Ser 225	Ala	Thr	Ile	Cys	Arg 230	Gln	Pro	Ser	Thr	Pro 235	Gln	Arg	Arg	Arg	Thr 240
Gln	Gln	Gly	Gln	Arg 245	Asn	Thr	Pro	His	His 250	Ser	Ala	Ala	Asp	Ser 255	Ser
Thr	Ala	Ser	Glu 260	His	Asp	Met	Val	Gly 265	Ile	Ser	Ser	Ala	Phe 270	Asn	Ala
Ala	Cys	His 275	Met	Leu	Lys	Arg	Val 280	Ala	Pro	Thr	Glu	Ala 285	Thr	Val	Leu
Phe	Thr 290	Gly	Glu	Ser	Gly	Val 295	Gly	Lys	Glu	Met	Phe 300	Ala	Arg	Met	Leu
His 305	Arg	Ile	Ser	Pro	Arg 310	His	Asp	Gly	Pro	Phe 315	Val	Ala	Val	Asn	Cys 320
Ala	Arg	Ile	Pro	Glu 325	Thr	Leu	Met	Glu	Ser 330	Glu	Leu	Phe	Gly	Val 335	Glu
Arg	Gly	Ala	Phe 340	Thr	Gly	Ala	Thr	Gln 345	Ser	Arg	Ala	Gly	Arg 350	Phe	Glu
Arg	Ala	Ser 355	Gly	Gly	Thr	Leu	Phe 360	Leu	Asp	Glu	Ile	Gly 365	Thr	Leu	Ser
Leu	Val 370	Ala	Gln	Gly	Lys	Leu 375	Leu	Arg	Ala	Leu	Gln 380	Glu	Ser	Glu	Val
Glu 385	Arg	Val	Gly	Gly	Ser 390	Arg	Thr	Leu	Lys	Val 395	Asp	Val	Arg	Val	Val 400

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Ala Ala Thr Asn Val Asp Leu Arg Ala Gly Val Gln Arg Gly Glu Phe 405 410

Arg Glu Asp Leu Phe Phe Arg Leu Asn Val Tyr Pro Ile His Leu Pro 420

Pro Leu Arg Glu Arg Lys Glu Asp Ile Pro Leu Leu Met Thr Tyr Phe

Leu His Arg Phe Asn Gln Arg His Ser Arg Val Val Ser Gly Phe Thr 450 455

Pro Arg Ala Ala Asn Ala Leu Leu Gly Tyr Asp Phe Pro Gly Asn Ile 475

Arg Glu Leu Gln Asn Leu Val Glu Arg Gly Val Ile Ser Ala Pro Glu

Asp Gly Ala Ile Asp Val Ser His Leu Phe Thr Ser Gly Glu Arg Leu 500 505

Thr Gln Pro Met Phe Ser Ile Gly Ala Ser Gly Ile Leu Ala Thr Ala 520

Gln Asp Asn Gln Pro Gln Glu Thr Gly Ser Pro Ser Thr Ser Phe Ser 535 530

Lys Pro Thr Ser Thr Ile Asp Ser Pro Leu Asp Ser Lys Asp Leu Ser

Ala Met Thr Leu Gln Glu Val Glu Asp Ala Met Ile Ser His Ala Leu 565 570

Gly Gln Val Lys Gly Asn Val Ser Glu Ala Ala Arg Arg Leu Gly Leu 585 580

Thr Arg Ala Gln Leu Ser Tyr Arg Ile Ser Arg Arg Pro Leu Asp Lys 605 595 600

- (2) INFORMATION FOR SEQ ID NO: 41:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 768 base pairs
 - (B) TYPE: nucleic acid (C) STRANDEDNESS: double

 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

770

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,	1 5	37	U	71	TITT	TD	T.	

(A) NAME/KEY: CDS

(B) LOCATION: 1..765

(D) OTHER INFORMATION:/product=

"Coniferylalkohol-Dehydrogenase" /gene= "cadh"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

	CAA Gln 610															48
	GGT Gly															96
	GGC Gly															144
	GCT Ala															192
	CCG Pro															240
	GCC Ala 690															288
	CTG Leu															336
	AAC Asn															384
	CAT His															432
	CTT Leu															480
AAA	GAA	GCA	CTG	ATC	GTT	TGG	TCT	CAA	GTT	CAG	GCG	CAG	GAA	TGG	TTC	528

Lys Glu Ala Leu Ile Val Trp Ser Gln Val Gln Ala Gln Glu Trp Phe

780

775

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ATG Met 785	AGG Arg	ACG Thr	TCT	GTA Val	CGC Arg 790	ATG Met	AAC Asn	TGC Cys	ATC	GCC Ala 795	CCC Pro	GGC Gly	CCT Pro	GTA Val	TTC Phe 800		576
ACT Thr	CCC Pro	ATT Ile	CTC Leu	AAT Asn 805	GAG Glu	TTC Phe	GTC Val	ACC Thr	ATG Met 810	Leu	GGT Gly	CAA Gln	GAG Glu	CGG Arg 815	ACT Thr		624
	GCG Ala																672
GCC Ala	GCG Ala	GTG Val 835	ATT Ile	GCA Ala	TTC Phe	ATG Met	TGT Cys 840	GCT Ala	GAG Glu	GAG Glu	TCA Ser	CGT Arg 845	TGG Trp	ATC Ile	AAC Asn		720
	ATA Ile 850																765
TAA																	768
(2) INFORMATION FOR SEQ ID NO: 42:																	
	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 255 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear																
	(ii) MOLECULE TYPE: protein (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:																
Met l	Gln	Leu	Thr	Asn 5	Lys	Lys	Ile	Val	Val 10	Thr	Gly	Val	Ser	Ser 15	Gly		
Ile	Gly	Ala	Glu 20	Thr	Ala	Arg	Val	Leu 25	Arg	ser	His	Gly	Ala 30	Thr	Val		
Ile	Gly	Val 35	Asp	Arg	Asn	Met	Pro 40	Ser	Leu	Thr	Leu	Asp 45	Ala	Phe	Val		
Gln	Ala 50	Asp	Leu	ser	His	Pro 55	Glu	Gly	Ile	Asp	Lys 60	Ala	Ile	Ser	Gln		
Leu 65	Pro	Glu	Lys	Ile	Asp 70	Gly	Leu	Cys	Asn	Ile 75	Ala	Gly	Val	Pro	Gly 80		
Thr	Ala	Asp	Pro	Gln 85	Leu	Val	Ala	Asn	Val 90	Asn	Tyr	Leu	Gly	Leu 95	Lys		
Tyr	Leu		Glu	Ala	Val	Leu		Arg	Ile	Gln	Pro	Gly	Gly	ser	Ile		

4.5

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- Val Asn Val Ser Ser Val Leu Gly Ala Glu Trp Pro Ala Arg Leu Gln 115 120 125
- Leu His Lys Glu Leu Gly Ser Val Val Gly Phe Ser Glu Gly Gln Ala 130 \$135\$
- Trp Leu Lys Gln Asn Pro Val Ala Pro Glu Phe Cys Tyr Gln Tyr Phe 145 \$150\$ \$150\$ \$155\$
- Lys Glu Ala Leu Ile Val Trp Ser Gln Val Gln Ala Gln Glu Trp Phe 165 170 175
- Met Arg Thr Ser Val Arg Met Asn Cys Ile Ala Pro Gly Pro Val Phe 180 185 190
- Thr Pro Ile Leu Asn Glu Phe Val Thr Met Leu Gly Gln Glu Arg Thr 195 200 205
- Gln Ala Asp Ala His Arg Ile Lys Arg Pro Ala Tyr Ala Asp Glu Val $210 \ \ 215 \ \ 220$
- Ala Ala Val Ile Ala Phe Met Cys Ala Glu Glu Ser Arg Trp Ile Asn 225 230230235
- Gly Ile Asn Ile Pro Val Asp Gly Gly Leu Ala Ser Thr Tyr Val $245 \\ 250 \\ 250$